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CLINICAL USE OF AMINO ACIDS FOR THE MAINTENANCE OF NITROGEN EQUILIBRIUM

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DETROIT

It has previously been shown that a mixture containing all the essential amino acids can be administered parenterally without untoward effect, that amino acid mixtures so administered may be substituted for protein in the diet and that by this means a patient may be maintained in nitrogen equilibrium.[1] It has also been shown that the solution may be administered at the rate of 1 to 2 Gm. of amino acid nitrogen an hour and that, so administered, over 95 per cent of the amino acids was utilized in patients with malignant growths, hyperthyroidism, hypothyroidism, chronic infections, chronic nephritis or cirrhosis of the liver.[2]

The present study was undertaken to extend the types of conditions in which solution of amino acids may be profitably used and also to observe the effect of this amino acid solution on the blood protein and blood amino acid level. The solution was administered orally, intravenously and intrasternally. The material used was an acid hydrolysate of casein with 1 per cent tryptophane added for parenteral use and an enzymatic hydrolysate for oral use. It is a 15 per cent solution containing 2.1 per cent nitrogen and was prepared by Sahyun.

For intravenous administration, the amino acid solution may be diluted in two or three parts of isotonic solution of sodium chloride, or in 5 or 10 per cent dextrose. The rate may be as rapid as 200 cc. of the amino acid solution an hour, although this is influenced by the rate at which the diluent—for example, 10 per cent dextrose—can be given. In general, the rate is determined by the response of the patient. Should such symptoms as headache, flushing, dizziness or nausea arise, they may be abated by reduction of the rate of administration.

Injection of amino acid solution into the bone marrow was done intrasternally with Turkel needles. The method was used on 3 patients, and it was found that amino acids may be given by this route as rapidly as intravenously. The results were no different than those with the other methods, but intrasternal administration was advantageous in patients in whom access to the veins was difficult. The Turkel needles may be left in place for twenty-four hours or longer and repeated injections may be given through them.

For oral administration the amino acid solution was diluted in fruit juice or tomato juice. This method was just as effective as intravenous injection, and clinically the ingestion of protein nitrogen in the form of amino acids gave a better result than did a high protein diet.

USE OF AMINO ACIDS IN SURGICAL CASES

In operative conditions, such as gastric surgery, in which the patient can take nothing by mouth for considerable periods before or after operation, it is possible to maintain adequate nutrition by the parenteral administration of amino acid solution and 10 per cent dextrose. Three such cases are included in the present series:

CASE 1.—A man aged 70 after a posterior gastrojejunostomy was given intravenously 400 cc. (60 Gm.) of amino acid solution in 3,000 cc. of 10 per cent dextrose daily for five days. On the sixth day and daily thereafter he was given 200 cc. (30 Gm.) of amino acid solution in tomato juice plus a varying amount of protein in a soft diet. This continued until a gastric resection was performed one month after the first operation. Then postoperatively daily for the first three days the patient was given 200 cc. (30 Gm.) of amino acids in 3,000 cc. of 10 per cent dextrose. The patient made an uneventful recovery. Blood protein levels were maintained throughout.

CASE 2.—A man aged 58 at operation was found to have a large carcinoma of the stomach with extensive metastases to the liver and omentum. Preoperatively daily for five days he received 400 cc. (60 Gm.) of amino acid solution in 5 per cent dextrose. Postoperatively he was given 400 cc. intravenously daily for seven days and then 400 cc. intravenously and 200 cc. orally for twelve days. The patient died three weeks after operation. The blood protein levels were 6.6 Gm. per hundred cubic centimeters before operation, 4.7 Gm. per hundred cubic centimeters on the eighth day after operation and 6.1 Gm. per hundred cubic centimeters four days before death. The addition of the oral amino acids after the seventh day helped raise the blood protein level, but it did not reach normal.

CASE 3.—A man aged 26 was admitted with a diagnosis of acute appendicitis and was operated on the same day. He was found to have an acute ruptured appendix with diffuse peritonitis. He received 400 cc. of amino acid solution in 3,000 cc. of 10 per cent dextrose daily for the first six days. During this time he took nothing by mouth. For the next six days amino acid solution was given orally in fruit juice with a soft diet. The blood protein levels were 6 Gm. per hundred cubic centimeters on the first postoperative day, 6.1 Gm. per

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Amino acid solutions used in this study were furnished by Frederick Stearns & Co., Detroit.

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2. Altshuler, S. S.; Hensel, Hilda H.; Hecht, Paul, and Pursley, Richard: Arch. Int. Med., to be published.

hundred cubic centimeters on the seventh day, and 6.7 Gm. per hundred cubic centimeters on the fifteenth day. The patient made an excellent recovery.

During periods when these patients were taking nothing by mouth it was found to be most important that sufficient dextrose be given to supply the necessary

Fig. 1.—Varicose ulcer of five months' duration.

calories. Otherwise the amino acids would be utilized for energy instead of for tissue repair.

The second group consists of 7 cases of nonhealing postoperative wounds:

CASE 4.—A man aged 55 was operated on at another hospital for a ruptured gangrenous appendix, and the incision became infected. On admission a secondary closure was performed; four days later the wound was not healing and the peritoneum was visible. Intravenous administration of amino acid solution was begun and continued daily for eight days. Decided improvement was observed after four days of this treatment. Beginning with the ninth day, amino acids were given orally for six days. The wound continued to heal and the patient made a good recovery.

CASE 5.—A man aged 49 was operated on for umbilical and bilateral inguinal hernias. A separation of the umbilical and right inguinal incisions ensued, which were then reoperated on. Eight days later the wounds disrupted. Intravenous administration of amino acid solution was begun and continued for five days, after which the solution was given orally for eight days. A month later oral administration was resumed in preparation for a secondary closure, which was performed. Amino acid therapy was continued for five days. The following month the patient was discharged with wounds well healed.

CASES 6 and 7.—Two men with carcinoma of the penis had amputations performed and the wounds were healing very slowly for five weeks. One patient had a urethral transplant made beneath the scrotum. After the operation the margin of the transplant did not heal. Each patient was given daily 200 cc. of amino acid solution orally for nineteen days. In the case in which the transplant was made, the wound healed, the patient gained 2½ pounds (1,134 Gm.) and he was discharged feeling well. In the other case the wound healed satisfactorily.

CASE 8.—A man aged 79 had a perineal prostatectomy which was healing very slowly, and a fecal fistula developed. A month after operation daily oral administration of 200 cc. of amino acid solution was begun. An improvement was noted in the patient's general condition, and the wound healed more rapidly. The fistula was allowed to heal until a sinus tract developed. Two months later the sinus tract was resected and the wound healed well. In the two months preceding the second operation the patient gained 31 pounds (14 Kg.).

CASES 9 AND 10.—Two patients had sinuses following drainage of perinephritic abscesses. One patient had been operated on a month before amino acid therapy was begun. The other patient had been operated on five months before, the wound had healed and then ruptured to the surface over the flank about a month before. Daily oral administration of 200 cc. of amino acid solution was started and in four weeks the sinuses of both patients were completely closed.

NONHEALING ULCERS

Ten nonhealing ulcers were studied, 2 of them in diabetic patients:

CASES 11, 12, 13 and 14.—Four patients had varicose ulcers of the legs of from seven months' to two years' duration, one ulcer having recurred periodically for thirteen years. These patients were given daily 300 cc. of amino acid solution orally for four weeks, by which time all the ulcers showed definite improvement (figs. 1 and 2). One patient left the hospital and did not report to the clinic for his amino acid solution. Three weeks later a definite increase in the size of his ulcer was observed.

Fig. 2.—Same ulcer shown in figure 1 after two months' treatment with amino acid solution.

CASE 15.—A woman aged 64 had a decubitus ulcer of the leg due to pressure of a cast. Eleven months after removal of the cast the ulcer had not yet healed. She was given 300 cc. of amino acid solution daily for three weeks, by which time there was definite evidence of healing.

CASE 16.—A man aged 62 had a decubitus ulcer on the leg after removal of a cast. The condition had endured for six

months and the ulcer was spreading. Daily oral administration of 300 cc. of amino acid solution was begun and after five weeks the ulcer showed definite improvement.

CASE 17.—A woman aged 46 has a decubitus ulcer of the back of three years' duration. She has the tremor and facies of Parkinson's disease and has not walked for three years. Lying on her back has subjected the sacrum, knees and heels to constant pressure, which resulted in a large infected ulcer over the sacrum. Her daily temperature rises are to as high as 102 F. Oral administration of 300 cc. of amino acid solution was begun and has been continued daily. The patient showed improvement for five weeks, but during the past week the ulcer has become larger and her general condition is poor.

CASE 18.—A man aged 36, following gunshot wounds fourteen years ago, developed chronic osteomyelitis of the left ankle with ulcer. X-ray examination revealed rarefaction of the external malleolus. Two skin grafts were tried unsuccessfully. Amino acid therapy was given for three months, during which time the ulcer improved. When administration of amino acids was discontinued, however, the ulcer increased in size (figs. 3, 4 and 5).

CASES 19 and 20.—Two diabetic patients, a man and a woman aged 60 and 62 respectively, had ulcers of the feet; both had previously undergone amputation of the other extremity above

Fig. 3. (case 18).—Draining ulcer recurring intermittently for thirteen years, following gunshot wound.

the knee. The man had an ulcer on the lateral side of the foot of nine weeks' duration. The infection had been well cleaned but no healing was taking place. He was given 200 cc. of amino acid solution daily by mouth and in three weeks was able to return to his work as a timekeeper. The woman had an ulcer of the big toe in which healing was imperceptible, although it had been clear of infection for about five months. After four weeks of daily oral administration of 200 cc. of amino acid solution the ulcer was practically all filled in.

BURNS

Three cases of burns—2 of them extensive—were treated:

CASE 21.—A man aged 52 had an infected third degree burn on the dorsum of the right foot with lymphangitis and lymphadenitis, and also first and second degree burns on the left leg. For six weeks healing had been very slow. Oral administration of 400 cc. of amino acid solution was begun and continued daily for twenty-three days. The patient was discharged three weeks later with the burns nearly all healed.

CASE 22.—A man aged 37 for seven months had been treated for first, second and third degree burns involving the left upper arm, shoulder, upper half of the trunk and left thigh. He had a daily rise of temperature ranging from 102 to 104 F. The wounds were healing very slowly; they were tender, and the patient seemed quite toxic. Administration of 100 cc. of amino acid solution intravenously was started and continued daily for seventeen days; after this amino acid solution was given orally for three months, starting with 100 cc. daily and gradually increasing to 400 cc. daily. The patient improved rapidly, tenderness of the wounds disappeared and the burns healed very well (figs. 6 and 7). The blood protein remained at normal values throughout.

Fig. 4 (case 18).—Same ulcer after three months' treatment with amino acids.

CASE 23.—A woman aged 27 had extensive burns on both upper and lower extremities, neck and part of the chest. She had been treated at another hospital and skin grafts had been tried unsuccessfully. She was given 300 cc. of amino acid solution daily by mouth. The burns were healing fairly well but renal insufficiency developed and the patient died of uremia.

GASTROINTESTINAL CONDITIONS

Two patients had gastrointestinal conditions.

CASE 24.—A man aged 75 had diverticulosis of the colon and duodenum with bleeding, macrocytic hyperchromic anemia and

Fig. 5 (case 18).—Appearance of ulcer after amino acids had been discontinued for one month.

possible cirrhosis of the liver. He received a high protein diet, iron and 200 cc. of amino acid solution by mouth daily for three weeks. On admission liver function tests revealed impairment, but later they were normal. On admission, laboratory findings were hemoglobin 11.5 Gm. and red blood cells 2,940,000; after treatment they were hemoglobin 13 Gm. and red blood cells

4,010,000. The blood protein level before treatment was 5.3 Gm. per hundred cubic centimeters and after treatment 7.6 Gm. per hundred cubic centimeters. The patient was discharged much improved.

CASE 25.—A man aged 28 complained on admission of diarrhea with ten to twelve stools a day. The condition had

Fig. 6 (case 22).—Burns of seven months' duration.

persisted for about a year. He was given 200 cc. of amino acid solution by mouth daily for thirteen days and was discharged much improved.

MUSCULAR DYSTROPHIES

Four patients were seen with muscular dystrophies:

CASE 26.—A woman aged 48 with amyotrophic lateral sclerosis was not able to sit up at the time of admission. She was daily given 200 cc. of amino acid solution orally for a month, then 100 cc. orally for twelve days and since that time 200 cc. daily. She is now able to be out of bed, to walk and to help herself. The fibrillations are less pronounced.

CASE 27.—A man aged 34 has had amyotrophic lateral sclerosis since 1938 with progressive disability. On admission he was completely bedridden and unable to care for himself, since he could not lift his arms. He had definite dysarthria and dysphagia and very coarse, ubiquitous fibrillations. He could scarcely be understood when he spoke. He was treated with prostigmine, potassium chloride and vitamin C, none of which had any noticeable effect. He was given 200 cc. of amino acid solution intravenously daily for a month, after which administration was changed to oral. His condition improved to the point at which he was able to make himself understood, feed himself, smoke and tend to his personal needs. He is not able to walk but he can sit up without support. Fibrillations still persist, but atrophy has not progressed. When administration of amino acid solution was discontinued his condition rapidly reverted to the former state. He was again given intravenous amino acid solution daily with decided improvement.

CASE 28.—A man aged 52 had his condition diagnosed as amyotrophic lateral sclerosis three years ago, and since that time his course was downhill. He was given 200 cc. of amino acid solution intravenously daily for three weeks, after which the administration was changed to oral. The patient shows definite improvement and has maintained his weight.

CASE 29.—A man aged 52 had myatonia atrophica and diabetes; he was unable to take care of his own needs or even to turn over in bed without assistance. He was given 200 cc. of oral amino acid solution daily for two weeks, and the amount was then increased to 300 cc. a day. The patient now can eat alone, take care of his personal needs and sit in a wheel chair.

BLOOD STUDIES

Plasma protein levels were determined on every patient receiving amino acid solution. It was found that the plasma protein level can be elevated or maintained at normal with the administration of amino acid solution providing there are enough calories furnished by the diet or in the form of dextrose. Otherwise the amino acids will be utilized for energy rather than for plasma or tissue regeneration. There is clinical and experimental evidence that amino acids as the sole source of nitrogen can regenerate plasma protein [3] and can promote growth.[4]

The plasma protein levels did not always agree with the clinical results. Several patients who showed very

Fig. 7 (case 22).—Same burns after five months' treatment with amino acids.

fine clinical improvement did not have a corresponding rise in the plasma protein levels. This may be due to the influence on plasma protein levels of other factors.

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such as infection, the state of hydration or the amount of protein reserve in the tissues.[5]

The effect of the parenteral administration of the solution on the blood amino acid levels was also studied. Two male patients were given a diet containing 90 Gm. of protein, and the blood amino acids levels were determined by Sahyun's method[6] before breakfast and at intervals after meals. The levels were found to be constant. During the experimental period, a fasting level was determined before breakfast, and immediately after breakfast administration of 200 cc. of amino acid solution in 600 cc. of saline solution was begun. This took an hour and a half. Blood amino acid levels were determined half an hour after administration had been completed and at intervals thereafter for six and a half hours and are given in the accompanying table.

Blood Amino Acid Levels

	Mg./100 Cc.
Fasting	10.2
½ hour	10.5
1 hour	10.6
1½ hours	10.9
2½ hours	10.4
3½ hours	10.0
4½ hours	9.9
5½ hours	9.9
6½ hours	9.8

The small accumulation of amino acids in the blood following parenteral administration of the solution indicates rapid utilization. These results were similar to Sahyun's findings on rabbits.[7]

COMMENT

The significance of protein to the body has been universally recognized by chemists, physiologists and physicians. However, until recently nothing could be done to supply this essential to persons who were unable to take an adequate amount of protein by mouth. The ability to furnish protein to the body parenterally by the use of amino acids is a real advance in the field of nutrition.

In operative cases the assurance of an adequate supply of protein is most important, first, to protect the liver from possible toxic effects of anesthesia; second, to prevent tissue edema, which interferes with healing of the wound, and, third, to supply the essential nutrients required for tissue repair and regeneration.[8]

In the nonhealing ulcers and burns there was improvement in most cases after amino acid solution was given. The amino acids were not supplemented with vitamins because of the difficulty which would then arise in interpreting the results. For practical therapeutics, however, vitamins C and D should be used in conjunction with the amino acids to treat poorly healing wounds, ulcers and burns.

The clinical improvement of the patients with muscular dystrophies was quite striking. Problems still to be solved are how the amino acids produce this effect and why a relapse occurs when the amino acid therapy is discontinued.

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6. Sahyun, Melville: J. Lab. Clin. Med. **24:** 548 (Feb.) 1939.
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CONCLUSIONS

1. Solutions of amino acids were used as the only source of nitrogen during preoperative and postoperative periods.
2. Poorly healing postoperative wounds, ulcers and burns were stimulated to more rapid healing by the use of amino acids.
3. The disabling symptoms of muscular dystrophies were abated during the time that the patients were receiving amino acid solution.
4. Solutions of amino acids were found to be equally effective when administered orally, intravenously or into the bone marrow. The latter method done intrasternally offers an excellent way of achieving parenteral injection when the veins are inaccessible.

ABSTRACT OF DISCUSSION

MELVILLE SAHYUN, PH.D., Detroit: We have been studying amino acids since 1937. Nutritionally, amino acids are divided into two groups: (1) nonessential and (2) essential or indispensable. The latter consists of aliphatic amino acids (leucine, isoleucine, valine, methionene, threonine), basic amino acids (histidine, lysine, arginine) and aromatic amino acids (phenylalanine, tryptophan). While our knowledge of the indispensability of these amino acids is based on studies on animals, nevertheless we believe they are important and indispensable since the human system probably cannot synthesize them. One or more of these amino acids enters into the composition of different types of proteins. As an example, in insulin protein, the amino acid constituents of which are known, we find that it contains of the essential group leucine, histidine, arginine, lysine and phenylalanine. Casein of milk contains all the indispensable ones. The good clinical results reported in this article may be attributable in part to the presence of essential amino acids in the preparation administered to the patients. It is possible that under certain conditions we may not be able to make available, from the proteins of the diet, some essential amino acids required by the various organs of the body. As an illustration, a molecule of protein may be likened to a table or a chair and the parts of each to amino acids. A carpenter equipped with proper tools (enzymes of the body) can convert a table to a chair, provided he has all the essential parts, or in a simpler way can build a chair or a table from prefabricated parts—amino acids.

DR. HARRY KOSTER, Brooklyn: I thought it might be interesting to add experiences with 25 cases in which nitrogen excretion was studied preoperatively and postoperatively. The patients were starved for three days before operation. The urine was collected and the total nitrogen was estimated. Then operation was performed. They received nothing for five or six days subsequent to the operation except dextrose and 120 Gm. of amino acids administered intravenously daily. The total urine was estimated subsequently for total nitrogen and we found that it was possible to keep these patients in nitrogenous equilibrium. It seems to me that that is the important contribution that can be made at the present time. From a clinical standpoint one should be cautious about this sort of treatment. While, on an a priori basis, it might be considered that the supply of amino acids intravenously would be a beneficial thing, I don't think there is enough evidence to warrant any great enthusiasm. The important thing is that it is possible to keep a patient in nitrogenous equilibrium without providing transportation of the amino acids through the mucous membrane.

DR. SAMUEL S. ALTSHULER, Detroit: The cases which were presented are merely examples of early observations, and I feel that we should study more cases over longer periods of time. There are many other possible uses of amino acids yet to be investigated. By giving proteins intravenously, deaminization in the liver and absorption in the intestinal tract are eliminated. This may be the explanation of why administration of amino acids gives better clinical evidence of protein utilization than does ingestion of a high protein diet. However, this is among the problems yet to be worked out.

CUTANEOUS CHANGES IN THE SPRUE SYNDROME

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The sprue syndrome has become familiar to physicians everywhere through the large literature [1] which has accumulated since its original descriptions by Hillary in 1759, and independently by Manson and by Van der Burg in 1880. While sprue is common in certain tropical countries, which accounts for the designation "tropical sprue," recent publications by American and European authors have emphasized the importance of sprue as a widespread and frequently unrecognized disease of the temperate zone. From the many conflicting opinions of the past, two fundamental concepts regarding the nature of sprue have emerged: (1) that celiac disease in children, tropical sprue and nontropical sprue are variations of a single disease complex, the sprue syndrome,[2] and (2) that sprue is a disease often due to nutritional deficiency.[3]

Lesions of the tongue and oral mucous membranes in sprue have been well described and are regarded as of great diagnostic and prognostic importance by clinicians who have had wide experience with this disease. On the other hand, the often striking cutaneous changes have aroused relatively little attention, possibly because the widespread systemic disturbance overshadows the alterations in the skin. While resemblance is often superficial, and confusion is usually eliminated by careful consideration of accessory data, the cutaneous changes in the sprue syndrome are to be differentiated from such pigmentary disorders of the skin as hemochromatosis, acanthosis nigricans, Addison's disease, arsenical pigmentation, xeroderma pigmentosa, chloasma and lentigo.

GENERAL CONSIDERATIONS [4]

Sprue is a chronic disease the clinical picture of which varies with its duration and with its characteristic remissions. The insidious onset of sprue symptoms is usually preceded by a long period of dietary imbalance consisting in a deficiency of proteins and an excess of carbohydrates and fats. Gradually there is progressive weakness, asthenia, irritability, mental depression, weight loss with muscular wasting and loss of the subcutaneous fat, abdominal discomfort, diarrhea with the passage of numerous grayish, bulky, frothy, fatty, foul smelling, soft or liquid stools, anemia, glossitis and stomatitis, and in many cases hyperpigmentation of the skin.

Early in the course of sprue the anemia may be of the hypochromic, microcytic type, gradually becoming a hyperchromic, macrocytic anemia indistinguishable from pernicious anemia. In contrast to pernicious anemia the stomach contains free hydrochloric acid in the majority of cases, a finding which is often of great differential value. Paresthesias occur in some patients, although posterolateral sclerosis such as is seen in pernicious anemia is rare. Children with celiac disease show a hypochromic, microcytic anemia.

The serum calcium and phosphorus are frequently low. Tetany and osteoporosis are seen in adult sprue, while in celiac disease there are rachitic changes, dwarfism and tetany.

Thaysen [5] has described a low blood sugar curve in sprue patients following ingestion of 1.5 Gm. of dextrose per kilogram of body weight. This test is useful in differentiating sprue from other conditions with which it may be most easily confused.

The pathologic changes in sprue are not impressive.[6] The fatty tissue of the body is depleted, and there is atrophy and sometimes ulceration of the mucosa of the digestive tract.

Sprue responds dramatically to oral and intramuscular liver extract if treatment is not so long delayed that irreversible changes occur. The appetite returns, diarrhea ceases, the lingual papillae regenerate, and the patient gains weight and strength. There is a rise in reticulocytes in the circulating blood, and, with the assistance of iron, a normal blood picture is established.

LESIONS OF THE MOUTH AND TONGUE

Lesions of the oral mucous membranes are found in the majority of sprue patients. It has been suggested by Manson [7] that these mucosal changes reflect similar alterations in the entire digestive tract. Of the 34 cases of sprue collected by Thaysen [5] there was stomatitis in 26. From a study of 92 patients, 77 of whom had symptoms related to the tongue, Castle and his co-workers [3] concluded that a diagnosis of sprue is almost impossible in the absence of glossitis and digestive disturbances.

According to Thaysen,[5] stomatitis occasionally is a presenting symptom but usually appears after the onset of diarrhea. He found stomatitis localized principally on the tongue, manifested by swelling and redness of the individual papillae in a limited area at the tip of the tongue, or on the lateral margins. Often there was burning and smarting of the tongue and troublesome salivation. The intensity of symptoms varied greatly and was apparently unrelated to remissions and exacerbations of the disease.

In Thaysen's cases the formation of aphthae was rare. When it occurred it was most often on the lateral edges of the tongue, less frequently on the inferior surface of the tongue and buccal surface of the lips. Manson-Bahr and Willoughby,[8] however, found small aphthae on the buccal mucosa and tongue in 45, or 22.5 per cent, of 200 cases; and Low [9] described aphthae in 101, or 67 per cent, of 150 cases.

Bahr [10] has described the sequence of events taking place in the tongue. The sides and tip of the tongue were first involved, with inflammation and swelling of the fungiform papillae. Minute ulcers appeared, which after healing left areas in which papillae were absent.

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The filiform papillae disappeared, and fungiform papillae became visible as prominent red spots. In 2 cases observed by these authors, hemorrhages occurred in the corium of the fungiform papillae, forming hemorrhagic vesicles. Finally the fungiform papillae were destroyed. Longitudinal and transverse fissures appeared, and fissuring occurred at the corners of the mouth. Post-

Fig. 1.—Right anterior tibial region, showing rough, dry, hyperpigmented skin, with more deeply pigmented macular lesions.

mortem microscopic examinations of two sprue tongues showed atrophy of the lingual papillae with only the bases of the fungiform papillae remaining. There was denudation of the surface epithelium and invasion of yeast cells. Mackie and Fairley,[6] however, found no penetration of the mucosa of the tongue with the hyphae of monilia.

CUTANEOUS CHANGES

It would appear from the literature that alteration of the skin in sprue occurs in a high percentage of cases. This aspect of the disease has received but scant attention.

Bahr [10] described a dark brown, irregular, patchy pigmentation resembling exaggerated freckles, distributed to the forehead, cheeks, abdomen, anterior thighs, legs and scapulas.

According to Thaysen [5] the skin in sprue is pale, grayish yellow or yellow brown but not icteric, dry, without turgor and slightly scaly. Cutaneous pigmentation was noted in 12 of his 34 cases. In 5 cases there were diffuse, scattered brown patches. Two cases resembling chloasma, with pigmentation localized to the face. In 2 cases pigmentation was localized on the abdomen. In 1 case pigmentation was so deep that the case resembled Addison's disease. One patient had dark brown spots, 2 cm. in diameter, scattered over the entire body. Three severely anemic patients had petechiae. Brittle, frayed nails in 2 cases, and edema of the skin were also mentioned by this author.

Skin lesions were noted in 7 of 15 cases reported by Bennett, Hunter and Vaughan.[11] The eruption in several cases was confused with psoriasis, pustular dermatitis and eczematoid dermatitis. In 1 case there were large moist, red abraded areas 2 to 8 cm. in diameter with scaly, brown pigmented borders which resembled pellagra and cleared up after three weeks' treatment with brewers' yeast. In this case the skin lesions were so severe as to be the presenting symptom.

Snell [12] has commented on the resemblance of the hyperpigmentation of sprue to pellagra and acanthosis nigricans. Only 10 of 32 cases studied showed no pigmentation. In the remaining 22 cases there were pigmentary eruptions of varying degree. Petechiae were noted in 2 cases. In 2 cases there was eruption resembling pellagra. Diffuse melanosis was present in 1 case. Urticaria occurred in 1 case. Lackluster hair, brittle nails and clubbed fingers were common.

Thaysen,[13] in a series of 10 cases of sprue, described 7 in which symmetrical hyperpigmented patches occurred on the forehead and the nose and below the eyes. In several of these cases pigmented patches were present on the cheeks, and pigmented streaks from the angle of the jaw to the cheeks. Distribution of the eruption in 2 cases was so characteristic as to suggest the diagnosis.

A diagnosis of sprue was made in 6 cases studied in the medical service of the University of Virginia Hospital between 1927 and 1940. The records of these cases were reviewed.

Glossitis was noted in 5. In 2 no pigmentary changes in the skin were described. Four cases showed decided cutaneous changes characterized by inelasticity, dryness and scaling of the skin. In 1 a patchy brownish, pigmentary eruption was present on the extensor surfaces of the arms, legs and dorsum of the hands. One case showed universal yellowish pigmentation with hyper-

Fig. 2.—Face, showing chloasma-like eruption.

pigmented patches on the dorsum of the hands. One case showed generalized yellowish pigmentation. The case reported displayed universal pigmentation with superimposed localized hyperpigmentation.

11. Bennett, T. I.; Hunter, Donald, and Vaughan, Janet M.: Idiopathic Steatorrhea (Gee's Disease): A Nutritional Disturbance Associated with Tetany, Osteomalacia and Anemia, Quart. J. Med. **1**: 603 (Oct.) 1932.

12. Snell, A. M.: Clinical Observations on Nontropical Sprue, South. M. J. **28**: 516 (June) 1935; Tropical and Nontropical Sprue (Chronic Idiopathic Steatorrhea): Their Probable Interrelationship, Ann. Int. Med. **12**: 1632 (April) 1939.

13. Thaysen, T. E. H.: Ten Cases of Idiopathic Steatorrhea, Quart. J. Med. **4**: 359 (Oct.) 1935.

Autopsies were performed on 2 of the 3 patients who died. No significant changes were noted in the adrenals of these patients, 1 of whom had pigmentary changes; in the other no cutaneous changes were described.

While 6 cases do not represent a large experience, consideration of the clinical and histopathologic studies in 1 case has afforded an opportunity to form certain conclusions regarding the nature of the cutaneous changes in sprue.

REPORT OF CASE

A white married woman aged 26 was admitted to the medical service of the University of Virginia Hospital on Oct. 26, 1940 complaining of weakness and of numbness and tingling in the arms and legs of two and one-half years' duration. Weakness and fatigability increased, accompanied by pallor of the skin and severe transitory pains in the lower legs. These symptoms progressed with occasional remissions and exacerbations until April 1939, at which time she began to experience severe precordial pain, with exertional dyspnea and palpitation, requiring bed rest. In April 1940 the patient had a rapid onset of persistent diarrhea accompanied by abdominal distention, with the passage of four to eight bulky, foul smelling, soft or liquid stools daily. In June 1940 she began to experience soreness of the mouth and tongue, bleeding of the gums and painful ulcers of the mouth and tongue. At this time she noticed her skin becoming darker, with a brownish patchy eruption on the face, shoulders, arms and legs.

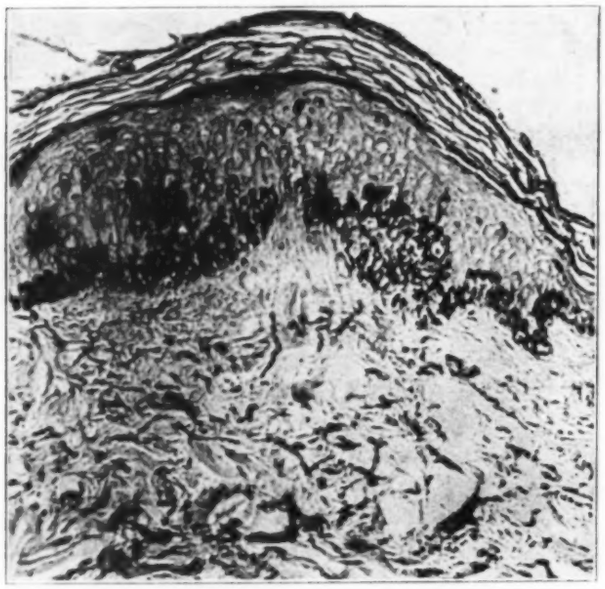

Fig. 3.—Section of skin of right lower leg, showing heavy deposits of pigment in the rete and basal cell layers. Foot's silver technic.

In spite of a good appetite and a diet containing adequate amounts of milk, eggs, fresh meat and vegetables (according to her story) she experienced a weight loss of 20 pounds (9 Kg.) during her illness.

The family, marital and past histories were irrelevant.

On admission the temperature was 100.1 F., the pulse rate 100, the respiratory rate 22 and the blood pressure 90 systolic and 60 diastolic. The patient was extremely emaciated. The skin was loose, rough and dry with universal yellow brown pigmentation. There were numerous irregular, discrete and confluent patches of deep brown pigmentation varying from 0.5 cm. to 5 cm. in diameter, symmetrically distributed to the cheeks, nose, scapular regions, extensor surfaces of the forearms and lower legs, and dorsum of the hands and feet. There were confluent hyperpigmented patches on the forehead and malar regions resembling chloasma. The mucous membranes were pale. The tongue was red and slick, and the fungiform and filiform papillae were absent. There was decided gingivitis. The cervical lymph nodes were palpable. The lungs were normal. There was a soft murmur following the first heart sound, heard best in the third left interspace. Rhythm, size, shape and position of the heart were normal. The tip of the spleen was palpable. The deep reflexes of the knees and ankles were hyperactive. Neurologic examination was otherwise normal.

The hemoglobin was 5 Gm. per hundred cubic centimeters (Haden), red blood cells 1,620,000, white blood cells 6,400 with 61 per cent polymorphonuclears, 2 per cent eosinophils, 28 per cent small lymphocytes, 3 per cent large lymphocytes and 6 per cent monocytes. Reticulocytes were 9.4 per cent. The color index was 1.08. The volume index was 1.2, hematocrit 16. The average cell size was 8 microns. There were numerous macrocytes in the stained blood smear. The blood Wassermann and Kahn reactions were normal. The urine was normal. Gastric analysis showed 45 degrees of free hydrochloric acid after subcutaneous injection of histamine. The icterus index was 10. Serum calcium was 10.3 mg., and phosphorus 6.4 mg. per hundred cubic centimeters. Plasma chlorides were 620 mg. per hundred cubic centimeters. The blood proteins totaled 5.8 Gm. per hundred cubic centimeters. Fasting blood sugar was 100 mg. per hundred cubic centimeters. A test for dextrose tolerance (oral) showed a "flat" curve with a maximum rise of 92 mg. per hundred cubic centimeters after one hour. A test for adrenal insufficiency, as standardized by Cutler, Power and Wilder,[14] was well within the limits of normal, with 10 mg. of chloride ion per hundred cubic centimeters of urine obtained on the specified routine. Sudan III stains on the stool showed definite increase in fat. Roentgenograms of the gallbladder and gastrointestinal tract disclosed no abnormalities.

The patient's temperature and pulse rate became normal within twenty-four hours after admission. On intramuscular and oral liver extract the reticulocytes rose to 12 per cent and the patient gained weight (5¼ pounds, or 2.4 Kg.) and strength. During her stay she passed from one to four stools daily except during the period of preparation for a gastrointestinal series, when she passed eight stools.

At the time of discharge, Nov. 22, 1940, the hemoglobin was 10 Gm. (Haden), red blood cells 3,120,000, white blood cells 7,800, color index 1.1, volume index 1.3, hematocrit 35, average cell size 7.5 microns, reticulocytes 0.9 per cent. The diffuse patchy pigmentation of the face, shoulders and extremities had diminished considerably at the time of discharge. Examination one month after she left the hospital revealed a 50 per cent diminution in the intensity of the generalized pigmentation with the disappearance of many of the larger hyperpigmented patches. No further clinical observations have been possible.

HISTOPATHOLOGIC OBSERVATIONS

A biopsy was made on the lateral middle third of the right tibial region. The excised tissue included several deep brown, macular patches, with a generous portion of the less deeply pigmented surrounding skin. The lower legs were free of scars, varicosities and stasis dermatitis.

The following histopathologic data were based on microscopic studies of sections fixed in 10 per cent solution of formaldehyde and embedded in paraffin. The following stains and combination of stains were used: hematoxylin and eosin, Van Gieson's picric acid and fuchsin stain [15] for connective tissue, the prussian blue reaction (after Kyes) for hemosiderin,[16] counterstained with Mallory's basic fuchsin for hemofusin,[15] and Foot's silver technic [17] for melanin.

The cutaneous surface was thrown into numerous folds. There was slight, loosely lamellated hyperkeratosis. The stratum granulosum was normal. Sections of the tissue stained with

14. Cutler, H. H.; Power, M. H., and Wilder, R. M.: Concentrations of Chloride, Sodium and Potassium in Urine and Blood: Their Diagnostic Significance in Adrenal Insufficiency, J. A. M. A. **111**: 117 (July 9) 1938.

15. Mallory, F. B.: Pathological Technique, Philadelphia, W. B. Saunders Company, 1938.

16. Bensley, R. R., and Bensley, S. H.: Handbook of Histological and Cytological Technique, Chicago, University of Chicago Press, 1938.

17. Foot, N. C.: Useful Methods for the Routine Examination of Brain Tumors, Am. J. Path. **14**: 245 (March) 1938.

hematoxylin and eosin showed heavy deposits of light brown, finely granular pigment in the cells of the basal layer. At intervals in the basal cell layer the pigment concentration was more intense. In these areas, collections of pigment laden rete cells extended far upward in the malphigian layer, forming a lenticle. The presence of hemosiderin (iron) was not demonstrable by the special stain. The silver stain without counterstain showed many fine pigment granules stratified longitudinally throughout the stratum corneum. The rete cells contained small numbers of fine, round or ovoid pigment granules. The lenticular collections, already described, showed heavy pigmentation. There were many fine, round or ovoid pigment granules in the columnar basal cells, with concentration of pigment in the upper portion of the cell, "capping" the nucleus. A few dendritic cells, laden with pigment, were arranged between the palisade basal cells. No abnormalities were seen in the corium.

COMMENT

In sprue the glossitis, stomatitis and fissuring at the corners of the mouth (ariboflavinosis) respond favorably to liver extract and appear to be related to a deficiency of the vitamin B complex.

The role of avitaminosis in the production of pigmentary changes requires further investigation. Anorexia, the damaged intestinal mucosa and the rapid passage of intestinal contents through the digestive tract operate to produce an extreme degree of vitamin deficiency. There is no doubt that a deficiency of the fat soluble vitamins occurs in patients with steatorrhea.[18] Certain components of the skin changes in sprue, such as roughness and dryness of the skin with follicular keratosis, may be due to avitaminosis A. Some observers [19] have suggested that the low values for serum calcium and phosphorus may be due to failure of absorption of vitamin D and to interference with vitamin D manufacture in the skin.

There has been much speculation regarding the nature of the cutaneous pigment. Since the icterus index is rarely elevated,[20] excessive hemolysis appears to have little if any part in the production of pigment. In the case reported the icterus index of 10 was not regarded as significant. The skin pigment does not give the reaction for iron.

Thaysen [5] has reviewed the literature dealing with the relationship of sprue to inadequate functioning of the adrenal cortex. Pigmentation, hypotension and adynamia, which occur so constantly in Addison's disease, are also found in a high percentage of sprue cases. In sprue these symptoms subside during remissions, and, as Thaysen has pointed out, no anatomic changes have been demonstrated that would suggest that sprue gives rise to Addison's disease. The case reported shows no abnormality of that part of the adrenal cortex involved in electrolyte metabolism.

The histopathologic features of this case, showing an increase in the melanin content of the basal cell and rete layers, support Thaysen's theory [5] expressed in the following quotation: "The chemical nature of the pigment is as yet quite unknown, but I find it not unreasonable to regard this pigmentation as an increase of the normal skin pigment."

Differential diagnosis of cutaneous pigmentation in sprue should offer no great difficulties.

Glossitis, pigmentation and favorable response to liver extract are characteristics common to pellagra, sprue and pernicious anemia. In pellagra the body weight is usually maintained, anemia is seldom severe and the cutaneous erythema, scaling, fissuring and crusting are limited to surfaces exposed to irritation or to the sun's rays. Follicular keratoses and cheilitis due to riboflavin deficiency are frequently seen; diarrhea and neurologic changes are usually present. The histopathologic picture in pellagra varies according to the stage of the disease. There is perivascular cellular infiltration in the corium, hyperkeratosis, parakeratosis and increased pigmentation in the basal layer and sometimes atrophy of the corium and epidermis.

The skin of pernicious anemia is diffusely icteric. Microscopic examination shows the presence of iron pigment. Achlorhydria occurs in all cases, while gastrointestinal symptoms are relatively uncommon. Combined degeneration of the spinal cord, seen in 5 per cent of the patients with pernicious anemia, frequently indicates the diagnosis.

The clinical and histologic features of acanthosis nigricans, Addison's disease, hemachromatosis and arsenical pigmentation have been described in detail by Montgomery and O'Leary.[21]

Acanthosis nigricans may be easily differentiated from sprue pigmentation by the symmetrically distributed, verrucous, pigmented patches, which show a characteristic histopathologic picture, and by the frequently associated neoplasm.

The pigmentation of Addison's disease may be indistinguishable clinically and histopathologically from sprue. Pigmentation of the mucous membranes of the mouth in patients with Addison's disease may be of differential value. The tendency of patients with Addison's disease to excrete urine containing chloride in high concentration has been found of diagnostic significance.[14]

In addition to the systemic changes of hemachromatosis, microscopic examination of the skin discloses deposits of hemosiderin. Arsenical pigmentation may be differentiated from sprue by the history of arsenical medication and by chemical determination of the arsenic content of the skin and urine. Microscopically, arsenical pigmentation shows hyperkeratosis and atrophy with inflammatory reaction in the papillary portion of the corium, whereas sprue, Addison's disease, chloasma and lentigo show only an increase in melanin content. Xeroderma pigmentosum, which shows pigmentation, atrophy, hyperkeratosis and formation of cutaneous carcinoma, can be easily differentiated from sprue pigmentation.

SUMMARY AND CONCLUSIONS

Stomatitis and glossitis with papillary atrophy are a constant feature of the sprue syndrome.

In a high percentage of cases of sprue the skin is rough, loose, dry and universally hyperpigmented, with a superimposed hyperpigmented macular eruption resembling chloasma. While variations in the intensity of the eruption are to be expected, in its fully developed form the cutaneous changes may often suggest the diagnosis.

Histopathologic alterations, consisting of excessive deposits of normal skin pigment (melanin) in the rete and basal cell layers, are not specific.

18. Albright, Fuller, and Stewart, J. D.: Hypovitaminosis of All Fat Soluble Vitamins Due to Steatorrhea, New England J. Med. **223**: 239 (Aug. 15) 1940.

19. Hanes, F. M., and McBryde, Angus: Identity of Sprue, Non-tropical Sprue and Celiac Disease, Arch. Int. Med. **58**: 1 (July) 1936.

20. Weiss, Charles: Recent Literature on Tropical Sprue, Arch. Path. **6**: 885 (Nov.) 1928. Suarez, R. M.: Clinical and Hematological Review of Sprue Based on the Study of 150 Cases, Puerto Rico J. Pub. Health & Trop. Med. **14**: 157 (Dec.) 1938.

21. Montgomery, Hamilton, and O'Leary, P. A.: Pigmentation of the Skin in Addison's Disease, Acanthosis Nigricans, and Hemachromatosis, Arch. Dermat. & Syph. **21**: 970 (June) 1930.

ABSTRACT OF DISCUSSION

DR. J. LAMAR CALLAWAY, Durham, N. C.: Drs. Kaufman and Smith have thoroughly studied their series of sprue patients from an angle hitherto only casually observed. During the past five years I have observed some 10 patients with sprue, and although certain of these patients had rough, loose, dry, somewhat hyperpigmented skin I have not been impressed with anything approaching a specific cutaneous picture such as is presented, for example, by pellagra. In the majority of sprue patients there is a multiple vitamin deficiency, and the cutaneous lesions were many times merely a manifestation of a generalized avitaminosis and not specific for the sprue syndrome itself. A review of records of 65 patients who were studied at Duke Hospital by Dr. Fred M. Hanes revealed that only occasional mention of pigmentation and cutaneous changes was made other than that the skin was loose, dry and somewhat scaling; however, these records were made by the regular house staff, which was not particularly cognizant of the cutaneous changes or interested in them. In several instances pigmentation suggestive of chloasma localized over the face was noted, and in 1 case the skin was distinctly yellowish brown with a follicular hyperkeratosis over the body, giving to the skin a rough, coarse feel which was described as like that of a shark's skin. There was no actual erythema, but the shins and wrists presented a pigmented appearance. Several of the cases reported by Drs. Kaufman and Smith showed a yellowish pigmentation and the exact significance of this in their cases or ours is not clear. The stomatitis, glossitis and papillary atrophy appear at all times to be a constant feature of the sprue syndrome. I agree with their description of the signs and symptoms of the sprue syndrome, their interpretation of the etiologic factors responsible and their therapeutic regimen. It has been suggested that the atrophic condition of the subcutaneous tissue as a result of fat loss may be responsible in some way for the generalized cutaneous appearance of the patients. In the microscopic sections that I have reviewed, the general appearance is much the same as those described by the authors. There is some hyperpigmentation, atrophy of the entire skin and appendages, with a moderate round cell infiltration. I did not grasp the significance of the histologic picture, but in the future I will be more observing of the clinical and histopathologic features of sprue patients.

DR. HERMAN SHARLIT, New York: I will offer an explanation for hyperpigmentation under all circumstances in which it may occur, based on observations in cell metabolism in such cells as can normally produce pigment. A living cell naturally must have oxygen to survive. The oxygen that reaches the cell is chiefly acquired by the primary respiratory system, which gives us our ordinary system of cellular respiration and which we can readily measure by the manometric method. Any other system of reaction in the cell requiring oxygen takes second place to this primary system in the integral organism. However, as soon as a piece of tissue is removed from the body that tissue is moribund. It is dying, and the first system which begins to show the evidence of this morbidity is the primary respiratory system. As this system loses in power, loses in ability to operate at optimum, other systems requiring oxygen can then operate more effectively. In other words, as soon as the oxygen potential in the cell becomes reduced, some other systems requiring oxygen can be more effective. One of these systems involves the production of pigment, so that in metabolic experiments on skin, where an effort is made to minimize the amount of oxygen available to the cell, in other words, to render the oxygen potential in the cell lower, the effect is one of provoking pigment production in epidermal cells. It is possible —and we have demonstrated it in our laboratory—to provoke pigment production in biopsy skin tissue in an atmosphere of nitrogen just as effectively as in an atmosphere of oxygen; the meaning of this is that, in the laboratory procedure of accelerating pigment formation in epidermal cells, atmospheric oxygen is not necessary. In other words, while it is not an anaerobic process, the amount of oxygen that is actually required within the cell can best be utilized when the oxygen potential therein is at a minimum. I would ask those who observe pigmentation to see whether they cannot be clinically impressed with the fact that in these cases, whatever the disease in which hyperpigmentations occur, we are dealing with partial anoxemia in the tissues. In the cases just reported, in which desperation for air causes rapid respiration, the cells are operating under a state of partial anoxemia, and this status can readily explain the pigmentation in these cases; if correct, it will tend to explain most hyperpigmentation.

DR. PAUL GROSS, New York: Considering the skin changes in sprue from the dermatologic point of view, one can readily see from the clinical description by the authors and the histopathologic aspects outlined by Dr. Callaway that the pigmentary changes are associated with an inflammatory reaction of the skin. It was this combination which prompted Erich Hoffman to speak of melanodermitis toxica rather than of melanosis (Riehl) when describing the peculiar pigmentary changes observed in certain persons during the first world war. This disease was considered a nutritional disturbance, and I have in the last two years observed a patient who presented a typical picture of melanodermitis toxica. The hyperpigmentation was confined to the exposed parts, namely the dorsum of the hands, the extensor surface of forearms and the face, especially the perioral region. The patient had a macrocytic anemia but no clinical signs of intestinal sprue. She responded well to intramuscular liver therapy but had two mild relapses a few months after liver therapy had been discontinued. It is not possible to say what deficiency is responsible for the melanosis, but the disturbance of intestinal absorption in sprue apparently represents one of the mechanisms which produce these peculiar skin manifestations.

DR. E. MYLES STANDISH, Hartford, Conn.: Apparently sprue is not uncommon in some other parts of the country. At a clinic in New York an interesting case of sprue was shown. The cause was definitely multiple avitaminosis. The woman, a Greek restaurant owner, had been eating irregularly. The case, undiagnosed for several weeks, was first recognized by the extreme loss of weight and weakness. She had not only the red atrophic tongue but also the shark skin and some pigmentation. She failed to improve on a diet and with heroic doses of vitamin B complex. Thorough blood work was done, including frequent tests for fat and cholesterol. Daily fat estimations in the stool were made. Then they began to give vitamin A in large doses. They gave the amazing amounts of 5,000,000 units of vitamin A obtained by a new process. They found that this was the only factor along with a much reduced fat diet that controlled the patient. She is still being followed carefully by the Rockefeller Institute and the New York Hospital group.

DR. MERLIN T. R. MAYNARD, San Jose, Calif.: In considering all these cases of intestinal and absorptive deficiencies, in which we can include celiac disease, sprue, chronic diarrheas, colitis and pernicious anemia, we should consider why the patient has these symptoms. We should go into the patient's history and find out whether or not he had symptoms primarily which suggested an achlorhydria or whether his diet at that time was deficient. Sprue, one might say, is the end result of multiple vitamin deficiency and the picture as described today is one of the B complex deficiencies. One may see a dominant A deficiency factor or one may see a dominant nicotinic acid deficiency factor or a riboflavin deficiency factor, but the thing that one has to treat is the patient's absorptive ability, which many times is so damaged by atrophy that he cannot absorb these things by mouth and one has to use injections. Incidentally, this patient apparently also shows a C deficiency. I think that Dr. Gross will agree that the action of vitamin C and the oxidation process of cells is important in the production of pigment, but riboflavin is slow in its effect, nicotinic acid is rapid. If vitamins are given by mouth and there is considerable atrophy of the mucous membrane, one has to give the patient time to absorb them and then to regenerate the papillae. Finally more rapid absorption will begin until, if one is giving larger doses, they absorb so fast that the effect is of overdosage. The crude liver extract is more effective by injection than is the refined liver extract and is probably a better method of

handling these cases in the early treatment rather than pushing so much medication by mouth. Later when one begins to get papillae back on the tongue one may give the medicament by mouth and discontinue the injections. The whole thing is an internal medical problem primarily. It is necessary to correct the achlorhydria that is primary, correct the dietary deficiency and finally treat effectively and not with too small doses and with full consideration of the pathologic changes found.

DR. DUDLEY C. SMITH, Charlottesville, Va.: There are many interesting cutaneous and medical problems associated with this condition. The relationship to pernicious anemia, of course, is very close. Whether or not the "hemopoietic principle" in liver is the curative factor for sprue is not known. There are many other important problems and relationships to be worked out.

INSULIN RESISTANCE DUE TO INFECTION IN DIABETES MELLITUS IN MAN

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Infection is probably the most common of the several causes for insulin resistance in diabetes mellitus in man, but the mechanism of this phenomenon is not understood. There are several theories which have been advocated to explain this resistance: (1) decrease of endogenous insulin secretion by the pancreas,[1] (2) decrease of effectiveness of endogenous and exogenous insulin,[2] (3) increase of metabolic rate,[3] (4) greater glycogenolysis by the liver,[4] (5) increase of epinephrine secretion by the adrenal,[5] (6) decrease of insulin kinase secreted by the liver,[6] (7) increase of adrenal cortex secretion,[5] (8) increase of secretion by the anterior lobe of the pituitary gland,[7] (9) increase of secretion by the thyroid gland,[5] (10) decrease in ability of the skeletal muscles to form glycogen[8] and (11) increase of inhibitory action on insulin of the blood plasma.[9]

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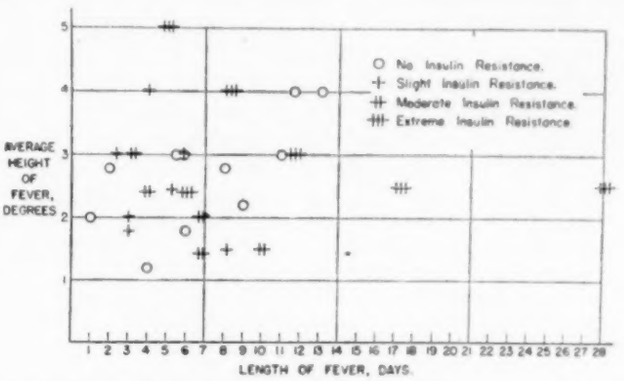
The present investigation was undertaken in hopes that the data might be of some value in understanding this mechanism. Therefore we studied the reaction of the diabetes in controlled cases to the following conditions: (1) different types of infection or idiopathic fever, (2) injections of foreign proteins, (3) fever induced by the cabinet method, (4) repeated administration of histamine and (5) repeated administration of epinephrine. The urine of all the patients used in this study was rendered free of sugar in the hospital before the infection or fever developed or the aforementioned methods of study were instituted.

There were 24 patients who contracted an infection or an idiopathic fever while in the hospital after the diabetes had been adequately controlled. Typhoid vaccine was administered intravenously in doses of from 1 to 60 million bacteria to 14 patients. Fever was produced by the cabinet method six times in 4 patients. Histamine was administered in doses of 1/40 grain (0.0016 Gm.) subcutaneously every four hours for two days to 2 patients, and epinephrine in doses of 0.5 cc. was administered intramuscularly every four hours for two days to 2 patients.

The degree of resistance was classified as slight, moderate and severe. If the insulin had to be increased 15 units or less to control glycosuria the resistance



Absence of apparent relationship between the presence or degree of insulin resistance and the average height and duration of the fever.

was called slight, an increase of 15 to 30 units was called moderate, and an increase of 30 or more units was called severe. In some instances the insulin was not increased or it was not increased sufficiently to prevent glycosuria. In such cases a glycosuria up to 20 Gm. was considered to be a slight resistance, 20 to 50 Gm. as moderate and above 50 Gm. as severe.

RESPONSE OF PATIENTS TO INFECTION

Of the twenty-eight observations on 24 patients who contracted infection or idiopathic fever, insulin resistance was not demonstrable in 10, whereas it was slight in 8, moderate in 4 and severe in 6. There was no apparent relation of sex, age or the duration of the diabetes to the development of insulin resistance. Mild or moderate diabetes, on the other hand, is more likely than severe diabetes to require more insulin during a toxemia, as shown in table 1. It is to be noted from table 2 that there was no relationship between the degree of fever and the degree of insulin resistance.

The greatest rise in body temperature may not be a good index of the severity of toxemia, because it may not persist for a sufficient time to alter the carbohydrate metabolism. It was for this reason that the average height of the fever and the degree of insulin resistance

were plotted with the duration of the fever. No definite relationship was observed. Two of the cases having the longest duration of fever also showed extreme increases of insulin requirement, but in one of these the insulin resistance had almost disappeared before the fever subsided. It is very common to observe insulin resistance appearing one to four days before any other evidence of infection; on the other hand, some cases do not require more insulin until several days after the infection is manifest, while in others the two appear simultaneously. In our cases the resistance developed before the fever in 2 instances, simultaneously with it in 5 and after in 9. There appears to be no relationship between the onset of insulin resistance and the onset of toxemia to the degree of alteration of insulin requirement.

The toxemia in 21 of our cases was due to infection, in 4 it was not due to infection and in 3 it was doubtful. A case of gastric hemorrhage due to a peptic ulcer presented a slight resistance and 1 with coronary occlusion a moderate resistance. All of the extremes occurred in cases of infection. Of the organisms known, streptococci were present in 5, tubercle bacilli in 1, Escherichia coli in 3 and pneumococci in 2. Not one of the infecting organisms showed any constant alteration of the insulin requirement. There was also no relation of the insulin sensitivity to the pathologic condition present, as shown in table 3. It is possible that the degree of toxemia is not measured accurately by the foregoing factors. It was for this reason that the mortality rate was compared with the presence and degree of insulin resistance. It is to be noted from table 4 that all of the patients showing slight insulin resistance

Table 1.—*Data Indicating That the Less Severe the Diabetes the More Likely That Extreme Insulin Resistance May Occur During Toxemia*

Severity of Diabetes	Insulin Resistance			
	None	Slight	Moderate	Extreme
Mild	1	2	..	3
Moderate	2	2	2	2
Severe	7	4	2	1

Table 2.—*Absence of Relationship Between Height of Fever and Degree of Insulin Resistance*

Degrees of Fever	Insulin Resistance			
	None	Slight	Moderate	Severe
0	..	..	..	..
1	..	..	..	..
2	..	2	..	..
3	4	2	1	..
4	3	3	1	3
5	3	..	1	1
6	..	1	1	1
7	..	..	..	1
Total	10	8	4	6

survived, death ensued in 1 case showing moderate and in 2 with no insulin resistance, whereas 4 of the 6 cases with severe resistance ended fatally. It is difficult to evaluate these 4 cases. In 1 of the 4 requiring great increases of insulin the resistance had almost disappeared before death, and in another the insulin requirement was not altered for the first twenty-three days but increased gradually during the last five days before death.

RESPONSE TO INTRAVENOUS ADMINISTRATION OF TYPHOID VACCINE

Of the 14 patients who received typhoid vaccine, 1 received two courses. The number of injections varied from one to ten in the different cases. In depancrea-

Table 3.—*Evidence That Insulin Resistance Is Not Related to Pathologic Condition Present*

Cause of Fever	Insulin Resistance			
	None	Slight	Moderate	Severe
Arsenical dermatitis	1	..	..	..
Coronary occlusion	..	..	1	..
Idiopathic	1	2	1	..
Gastric hemorrhage	..	1	..	..
Liver abscess	..	..	..	1
Infected thyroidectomy wound	1	..	..	1
Tonsillitis	1	1	..	..
Infected amputation stump	2	1	..	..
Miliary tuberculosis	1	..	..	..
Urinary tract infection	3	..	1	1
Lung abscess	..	..	..	1
Empyema	..	1	..	..
Pneumonia	..	..	..	1
Acute appendicitis	..	..	1	..
Panophthalmitis	..	1	..	..
Streptococcic infection, finger	..	1	..	..
Gangrene of toe	..	..	..	1
Total	10	8	4	6

Table 4.—*Data Indicating That Insulin Resistance Occurs More Frequently in Fatal Cases*

Outcome of Case	Insulin Resistance			
	None	Slight	Moderate	Severe
Recovery	8	8	3	2
Death	2	0	1	4

tized dogs Greene, David and Johnston [10] found that it was frequently necessary to administer typhoid vaccine repeatedly in some instances to produce insulin resistance, but the development of resistance was not related to the number of injections. Insulin requirement was not altered in 3 of the patients and was increased slightly in 6, moderately in 4 and extremely in 1. There was no relationship between the presence and degree of insulin resistance and the number of injections of typhoid vaccine, as shown in table 5. The presence and degree of insulin resistance were also not related to the height of the fever, as shown in table 6. An analysis of the response of each patient to each injection of typhoid vaccine revealed that slight insulin resistance developed even without the presence of fever. These data are shown in table 7. Of the 18 instances in which fever was not produced, a slight increase of insulin requirement was noted in 8. In those in which fever was produced there was no alteration of insulin requirement in 13, whereas varying degrees of resistance were present in 23 instances.

RESPONSE TO FEVER INDUCED BY CABINET METHOD

There were six observations on 4 patients whose diabetes had been controlled adequately before fever therapy. The effect of such therapy on the development of insulin resistance is shown in table 8. Insulin resistance developed to a slight degree during two of the

10. Greene, J. A.; David, Ann, and Johnston, George: Production of Insulin Resistance in Depancreatized Dogs, Am. J. Physiol. **136**: 595-599 (June) 1942.

six observations. One patient exhibited none during the first treatment but required a slight increase in insulin during the second. As in the previous groups there was no relationship between the height of the fever and the presence or degree of insulin resistance. Two of the patients had previously received typhoid vaccine, and their temperature curves were duplicated in the cabinet. It is of interest that 1 showed slight resistance following typhoid vaccine injection, but none with the fever therapy. The other patient acquired a severe resistance with typhoid vaccine, whereas it was only slight with fever therapy.

The insulin requirement of the 2 patients who received histamine or of the 2 who received epinephrine was not altered.

COMMENT

A decrease of endogenous insulin secretion by the pancreas is the theory which has been most widely accepted. The work of Greene, David and Johnston [10] which showed that insulin resistance can be produced in depancreatized dogs makes this theory untenable.

Another theory which has been fairly widely accepted is that the increase in metabolic rate accounts for the insulin resistance during an infection. Our observations cast a good deal of doubt on this theory. The presence and the degree of insulin resistance were not related to the height or duration of the fever in our cases with infection following typhoid vaccine administration or during and following fever induced by the cabinet method. In addition, some of our cases manifested slight resistance following typhoid vaccine injections without the appearance of fever, whereas, others showed none even though the body temperature rose 4 and 6 degrees. The difference in response of 2 cases to fever produced by typhoid vaccine administration and that produced by the cabinet method casts further doubt on this theory. These observations convince us that the fever is of minor significance in the production of insulin resistance. That the toxemia was more important has been suggested by Rabinowitch [11] and others and is supported by our observations. The term toxemia, however, is vague and does not explain the mechanism of this phenomenon. Depletion of the sugar stores of the body undoubtedly plays some role in certain cases of insulin resistance, as emphasized by Greene and Swanson,[12] but it is not the principal factor. An increase in the secretion by the thyroid has been thought to account for a greater insulin requirement, but Greene and Swanson [13] have previously shown that the hyperglycemia and glycosuria in cases of hyperthyroidism without diabetes mellitus can be eradicated by a diet high in carbohydrate and can be reproduced by a diet low in carbohydrate and high in fat.

Insulin resistance has been attributed to an increase of epinephrine secretion by the adrenal gland. It is generally recognized that hyperglycemia and glycosuria frequently follow the administration of epinephrine and in cases of pheochromocytoma, hyperglycemia and glycosuria are found during an attack of paroxysmal hypertension. The administration of epinephrine every four hours for two days in 2 of our cases, however, failed to produce any evidence of insulin resistance. It is readily admitted that the dosage may have been inadequate, but subjective and objective manifestations of epinephrine effect were produced in both cases. Such evidence is against insulin resistance being due to an increased epinephrine secretion by the adrenal gland.

The fact that the dogs described by Greene, David and Johnston [10] developed insulin resistance coincidentally with the greatest tissue reaction in a cellulitis produced by subcutaneous administration of turpentine suggests that a histamine-like substance may be liberated by the inflamed tissue and may be a factor in the

TABLE 5.—*Demonstration That Insulin Resistance Is Not Related to the Number of Typhoid Vaccine Administrations*

Number of Typhoid Injections	Insulin Resistance			
	None	Slight	Moderate	Severe
1	1	1	1	..
2	..	2	1	..
3	..	1	1	1
4	1	1	1	..
5	..	..	..	..
6	..	..	..	..
7	1	..	..	..
8	..	..	..	..
9	..	..	..	..
10	..	1	..	..
Total	3	6	4	1

TABLE 6.—*Demonstration That Insulin Requirement Is Not Related to the Height of Fever Produced by Administration of Typhoid Vaccine*

Degree of Fever	Insulin Resistance			
	None	Slight	Moderate	Severe
0	1	..	..	..
1	..	..	1	..
2	..	1	..	..
3	2	2	..	..
4	..	2	3	1
5	..	..	..	..
6	..	1	..	..
Total	3	6	4	1

TABLE 7.—*Response of the Diabetes to Single Injections of Typhoid Vaccine*

	Insulin Resistance			
	None	Slight	Moderate	Severe
No fever, no glycosuria	10	..	..	..
No fever with glycosuria	..	8	..	..
Fever without glycosuria	13	..	..	..
Fever with glycosuria	..	15	5	3

TABLE 8.—*Alteration of Insulin Requirement Produced by Fever Therapy by the Cabinet Method*

Degree of Fever	Insulin Resistance	
	None	Slight
4	1	1
5	..	..
6	1	..
7	2	1
Total	4	2

11. Rabinowitch, I. M.: Influence of Infection on Reaction of Diabetes to Insulin Treatment: Report of Unusual Case, Canad. M. A. J. **26:** 551-554 (May) 1932.

12. Greene, J. A., and Swanson, L. W.: The Utilization and Effect of Added Dextrose in Cases of Controlled and Uncontrolled Diabetes, J. A. M. A. **118:** 364-367 (Jan. 31) 1942.

13. Greene, J. A., and Swanson, L. W.: Alteration of Glucose Tolerance in Patients with Disease of the Pituitary, Thyroid and Adrenal Glands by Changes of Diet, J. Lab. & Clin. Med. **26:** 360-365 (Nov.) 1940.

production of insulin resistance. It was for this reason that histamine in mildly toxic doses was administered frequently for two days to 2 of our patients whose diabetes was controlled. There was no increase of insulin requirement in the 2 cases. These observations are against, but do not eliminate, the possibility that some such substance is a factor in the development of insulin resistance.

The importance of glycogenolysis by the liver in insulin resistance is still a debatable question. Newburgh and Conn [14] have postulated that an excess of fat in the liver is a factor in the glycosuria and hyperglycemia in cases of "fat diabetes." Soskin [4] has suggested that there is a greater glycogenolysis by the liver in insulin resistance. That a fatty liver was not a factor in insulin resistance in depancreatized dogs was shown by Greene, David and Johnston. [10] Soskin has attributed the glycogenolysis to an abnormal mechanism produced by an increase of amylase. Work recently completed in Gibson's [15] laboratory, however, failed to show any relationship between the blood amylase and the insulin requirement. In addition, one case of mumps pancreatitis in which the blood amylase was greatly increased failed to show hyperglycemia, glycosuria or decreased sensitivity to insulin.

It is difficult to evaluate the role played by the anterior lobe of the pituitary gland in alterations of insulin sensitivity. From the work of Young [7] and of Best and his co-workers [7] the action of the pituitary is on the pancreas. The production of insulin resistance in depancreatized dogs [10] casts some doubt on the role played by the anterior pituitary in insulin resistance of toxemias. The roles that are played by the liver, the pituitary, the adrenals and the muscles in the production of decreased sensitivity to insulin are yet to be established.

There is much to be learned regarding the mechanism of insulin resistance which occurs during infection in diabetes mellitus. Regardless of the mechanism there are a few pertinent observations worthy of note. Insulin resistance does not develop in all cases of diabetes mellitus during an infection. It may occur during one infection and not appear during another comparable toxemia. Insulin resistance is more likely to be developed by patients with less severe diabetes than by those with more severe diabetes. As a rule, however, those patients who develop extreme insulin resistance with one infection will also develop it with subsequent infections or fevers.

SUMMARY

The occurrence of insulin resistance has been ascertained in patients with diabetes mellitus during infections, idiopathic fever, administration of foreign proteins, fever produced by the cabinet method and administration of histamine and epinephrine.

Insulin resistance did not develop in all cases of infection or fevers or to administration of histamine or epinephrine. Its occurrence was not related to the sex, age, height and duration of the fever or to the apparent toxemia. Insulin resistance appeared to develop more frequently in mild than in severe cases. Different theories have been advocated to explain this phenomenon.

14. Newburgh, L. H., and Conn, J. W.: New Interpretation of Hyperglycemia in Obese Middle Aged Persons, J. A. M. A. **112**: 7-11 (Jan. 7) 1939.

15. Gibson, R. B.: Personal communication to the authors.

ABSTRACT OF DISCUSSION

DR. HOWARD F. ROOT, Boston: As the authors say, many different conditions may explain insulin resistance. The occurrence of insulin resistance calls attention to the need of further diagnostic study. Insulin resistance does not develop in all cases during infection. Actually, severe pyogenic infection sometimes lasts a long time, resulting even in death, and yet insulin resistance not only is absent but the patient, who previously required a large amount of insulin, may become during the last stages of his severe infection sugar free, with normal blood sugar, requiring no insulin. Dr. Valy Menkin of the Harvard Medical School has shown experimentally in diabetic animals that with pleural exudates, for example, there is a great excess in proteinolysis, so that the fluids in the affected area contain an excessive amount of amino acid nitrogen. Therefore the rise in blood sugar and the excessive glycosuria may be due to diffusion of dextrose from this area of increased protein breakdown. In a group with infection seen at the Deaconess Hospital, resistance to insulin has been associated with allergy to insulin. A patient who, in a previous admission, had a mild diabetes with only temporary use of insulin, returned with pyelitis. She required 80 to 90 units and had generalized urticaria whenever insulin was given. She was skin sensitive to the insulin molecule, but also in her blood serum specific precipitins to insulin were demonstrable. Her sensitization decreased and disappeared in the course of some months' time. Another young man, whose blood formerly showed no precipitin to insulin, developed precipitins to insulin and urticaria during the course of sarcoid of the lung. A third patient had had diabetes and asthma for many years. With the development of a slight attack of pneumonia, she became comatose and required 140 units. These cases justify the hypothesis that, in the presence of diabetes, an infection not merely may stimulate the antigenic mechanism in such a way as to produce antibodies to the specific invading organism but may stir up antibodies to insulin itself. This possibility is worthy of future study. Disturbances of glycogen storage and increased glycogenolysis occur in skin disorders and in liver disease with increase in insulin requirement. A woman with jaundice due to a stone in the common bile duct, at the time of the operation for the removal of the stone, required a thousand units a day, a few days later required none and now, two years later, still requires no insulin.

DR. JAMES A. GREENE, Iowa City: None of our cases showed any evidence of skin sensitivity to insulin. It seems difficult to believe that allergy is the important factor in cases with an infection lasting for four or five days, in which a severe insulin resistance develops. In such cases an insulin requirement of 15 units on a given potential sugar intake may increase to as much as 70 to 180 units for four or five days. Immediately after the fever subsides the insulin requirement decreases rapidly and within a week or ten days returns to the previous level. I can hardly see how allergy would explain that mechanism, but neither can I explain it by any other mechanism, so perhaps allergy is as good as any.

The Greatest Joy.—There are a few doctors who are disappointed in their profession. Their lives are busy, full of interest, and now and then exciting. New discoveries concerning the causes of disease, new methods, new drugs are constantly appearing; what was final six months ago has already been discarded. The doctor comes to know much of humanity—much more than does the priest, for in times of dire stress nothing is hidden from him—he sees men stripped of their bravado and women shorn of their blandishments; he may admire the courageous, but it is his greater privilege to comfort the frightened and discouraged. Some take pleasure in unraveling an obscure diagnosis, others in the exciting pursuit of an elusive scientific fact, most in the treatment and recovery of their patients. But the greatest joy of every true physician is to do each task well; 'his eyes look still upon the pattern of the thing that he maketh; he setteth his mind to finish his work, and watcheth to polish it perfectly.'—Irving, Frederick C.: Safe Deliverance, Boston, Houghton Mifflin Company, 1942.

MANAGEMENT OF MALE PUBESCENCE

FIRST LIEUT. WILLIAM A. SCHONFELD
MEDICAL CORPS, ARMY OF THE UNITED STATES

The period of pubescence and adolescence in a boy is frequently associated with physical and psychologic problems. Their solution frequently determines the effectiveness and happiness of the adult. It is the obligation of the general practitioner and pediatrician in cooperation with the school authorities, training centers for boys and the family to help solve these problems.[1] This requires an understanding of the mechanisms of pubescence and the ability to recognize and manage adequately their normal and abnormal variations.

MECHANISM OF PUBESCENCE

The development of a person includes a prolonged period of latency in genital growth called prepubescence (fig. 1 *A* to *B*).[2] During this time the testes do not grow but are maintained in this state of latency through the action of subthreshold amounts of hypophysial gonadotropic hormones.[3] During the second decade of life the anterior hypophysis through increased secretion in the quantity of gonadotropic hormones stimulates the interstitial cells of the testes to produce androgenic hormones. These in association with other factors of maturation induce rapid growth and development of the penis, prostate, seminal vesicles, larynx, hair follicles and epiphysis. This period of rapid genital growth is called pubescence [2] (fig. 1 *B* to *C*). The point in development when the testes have matured adequately to produce spermatozoa and the individual is capable of procreating is called puberty (*C*). Postpubescence or adolescence (*C-D*) follows this, with continued development of the primary and secondary sex characteristics to full maturity (*D*).

RANGE OF VARIATION

In view of the complexity of the process of growth and maturation it is not surprising to find great variations in normal boys [4] as to the age of onset of pubescence, the rate of development and the ultimate size of the genitalia. To determine the range of this variation I correlated the measurements of the penis and testes [5] with the degree of maturation of the secondary sex characteristics in about 1,500 males selected at random.

These subjects were then arbitrarily subdivided into six stages of development and maturation (fig. 2). The first stage included all the prepubescents and the sixth the adolescents and physically matured individuals, while the intervening stages included all the boys during pubescence. The qualifying criterion for the second stage was the beginning of active growth of the testes and penis but no pubic hair, while the third, fourth and fifth stages included respectively the three stages of pubic hair development described by Crampton.[2] In each stage I noted the range of size of the penis and testes as well as the associated secondary sex characteristics.

On the basis of this classification, the age frequency distributions were plotted for the 1,500 normal boys and men ranging in age from 1 day to 25 years (fig. 3). This chart indicates the decided variation as to physiologic development at each age. It illustrates that pubescence (stage 2) may normally begin at any age from 10 to 16, with isolated cases beginning even later, and the knowledge of the median or average age of onset is of no significance.[6]

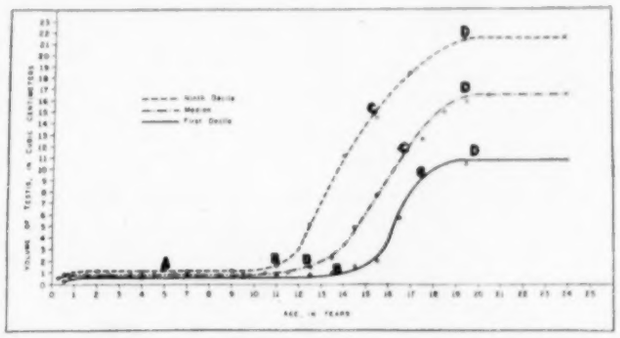


Fig. 1.—Phases of individual development: *A* to *B*, prepubescence; *B* to *C*, pubescence; *C* to *D*, postpubescence (adolescence). Point *C*, puberty; point *D*, maturity.

Cognizance of these variations of the normal [7] is one of the most important factors in the management of the male pubescent. By far the greatest number of prepubescents who are commonly regarded as endocrine problems will develop into normal adults,[8] whether the problem relates to the size of the genitalia, obesity or growth. This development is best achieved by wholesome surroundings among well adjusted adults, an adequately controlled diet and a well balanced ratio of rest and exercise, depending on the boy's needs.

PREPUBERAL OBESITY OR PSEUDO-FRÖHLICH SYNDROME

The most common problem that confronts the pediatrician and general practitioner interested in endocri-

From the Columbia-Presbyterian Medical Center and the Morrisania City Hospital, New York.

Read before the Section on Pediatrics at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

Released for publication by the War Department Manuscript Board, which accepts no responsibility, other than censorship, for the contents of this article.

Dr. Irving H. Pardee cooperated and actively participated in this study of male pubescence at Neurological Institute and Columbia-Presbyterian Hospital Medical Center during the past nine years. Dr. Max Gilbert of Schering Corporation supplied us with oretone, pranturon and anturon for this study.

1. Burns, D., and Secker, J.: Physical Fitness of Preadolescent Boys of Three Socio-Economic Levels, J. Physiol. **98:** 2P (March 14) 1940. Busing, H.: Ueber die körperliche Entwicklung Jugendlicher während der Lehrzeit (Ein Beiträg zur ärztlichen Berufsberatung), Gesundh. u. Erziehg. **49:** 34 (Feb.) 1936. Chambers, M. M.: Guidance for Rural Youth, Educ. Rec. **22:** 187, 1941. Frank, L. K.: Adolescence and Public Health, Am. J. Pub. Health **31:** 1143 (Nov.) 1941. Meyers, J.: Physical Findings in New York City Continuation School Boys: An Element in Vital Statistics of Adolescents, ibid. **21:** 615 (June) 1931. Pullias, E. V.: Maturation Factor in Vocational Guidance, School & Soc. **48:** 628 (Nov. 12) 1938. Schlesinger, E.: Jugendliche im Beruf. ihre körperliche Entwicklung während der Pubertät, Arch. f. Hyg. u. Bakt. **113:** 335, 1935.

2. Harris, J. A.; Jackson, C. M.; Paterson, D. G., and Scammon, R. E.: The Measurement of Man, Minneapolis, University of Minnesota Press, 1930, p. 215. Crampton, W. C.: Physiological Age: A Fundamental Principle, Am. Phys. Educat. Rev. **13:** 141, 214, 268 and 345, 1908.

3. Engle, E. T.: Action of Extracts of Anterior Pituitary and of Pregnancy Urine on Testes of Immature Rats and Monkeys, Endocrinology **16:** 506 (Sept.) 1932. Smith, P. E., in Allen, E.; Danford, C. H., and Doisy, E. A.: Sex and Internal Secretion, ed. 2, Baltimore, Williams & Wilkins Company, 1939, p. 931.

4. Moffett, C. W.: Shoe Sizing and Fitting: An Analysis of Practices and Trends, Miscellaneous Publication 469, United States Department of Agriculture, 1941. O'Brien, R.; Girshick, M. A., and Hunt, E. P.: Body Measurements of American Boys and Girls for Garment and Pattern Construction, Miscellaneous Publication 489, United States Department of Agriculture, 1941. Peter, Karl: Männliche, kindliche Geschlechts Organe, in Peter, Karl; Wetzel, Georg, and Heiderich, Friedrich: Handbuch der Anatomie des Kindes, Munich, J. F. Bergmann, 1928, vol. 2, pt. 1.

5. Schonfeld, W. A., and Beebe, G.: Variations in the Size of the Genitalia of Normal Boys from Birth to Maturity, to be published.

6. Greulich, W. W.; Day, H. G.; Lachman, S. E.; Wolfe, J. B., and Shuttleworth, F. K.: Handbook of Methods for the Study of Adolescent Children, Monographs of the Society for Research in Child Development, Washington, D. C., National Research Council, 1938, vol. 3, no. 2. Shuttleworth, F. K.: Adolescent Period (Graphic and Pictorial Atlas), ibid., no. 3; The Physical and Mental Growth of Girls and Boys Age Six to Nineteen in Relation to Age at Maximum Growth, ibid., 1939, vol. 4, no. 3.

7. Kubitschek, P. E.: Sexual Development of Boys with Special Reference to Appearance of Secondary Sexual Characters and Their Relationship to Structural and Personality Types, J. Nerv. & Ment. Dis. **76:** 425 (Nov.) 1932. Reich, H.: Klinische Testikelmessungen bei Kindern, Jahrb. f. Kinderh. **105:** 290, 1924.

8. Shorr, E.: Endocrine Problems in Adolescence, J. Pediat. **19:** 327 (Sept.) 1941.

nology is the management of the obese boy.[9] Since the distribution of fat in these boys resembles that found in women and adult eunuchs, the physician is inclined to make a diagnosis of obesity due to hypogonadism, particularly since the genitalia appear small. They fail to realize that this type of obesity is not at all abnormal in boys having a pyknic or predominantly endomorphic somatotype.[10]

The apparent hypogonadism is due to the fact that the penis is usually embedded in suprapubic fat. When the fat pad is pushed back (figs. 4 and 5) and the penis and testes are measured, it is evident that the genitalia are within the range of normal when compared to previously established standards[5] and that there is no delay in onset of pubescence.[11] Since there is no genital dystrophy, the diagnosis which is so frequently made of adiposogenital dystrophy of Fröhlich's type is entirely unwarranted. With the advent of puberty,

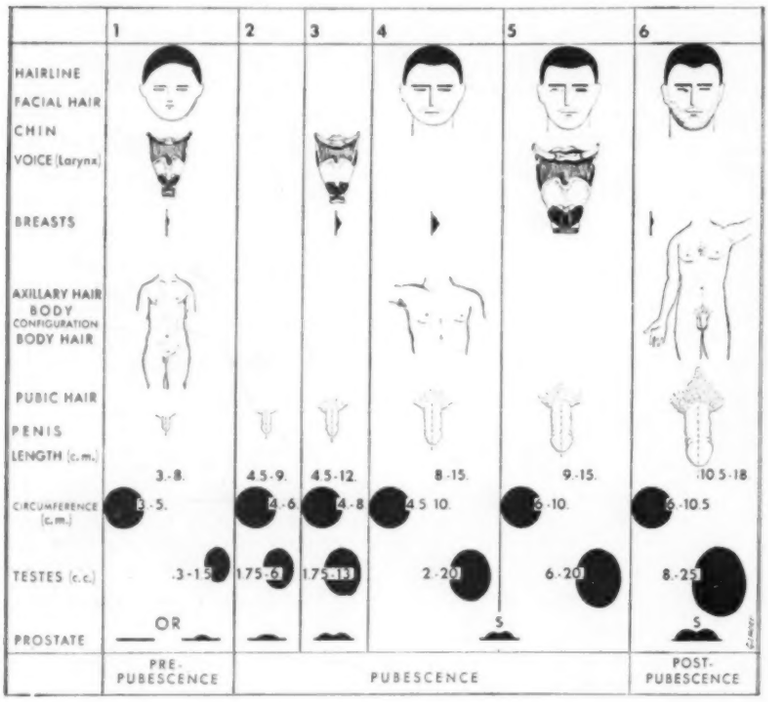


Fig. 2.—Stages of development and maturation.

most of these boys grow taller and slimmer,[12] although I believe they usually maintain their characteristic somatotype through life.

Thus, the treatment limits itself to a slimming regimen and the formation of new habits of activity and interests. Accordingly, to induce loss of weight[13] the diet should be reduced to the basal caloric requirements with a relatively high proportion of protein and supplementary vitamins and reduction of salts and fluids to a minimum. Although myxedema is uncommon, thyroid may be given along with the proteins to accelerate the basal metabolism. To be effective, desiccated thyroid must be given in the highest dose tolerated,[14] which is just below the toxic level for the individual. In addition, amphetamine sulfate may be used in 5 to 10 mg. doses morning and afternoon to dull insatiable appetites.[15]

RATIONALE OF ENDOCRINE THERAPY

The literature has created a great deal of confusion as to the indications, limitations and contraindications of the many commercially available potent endocrine products.[16] I shall attempt to clarify this situation by presenting a rational approach to the treatment of the problems associated with pubescence based on our controlled experiences in the endocrine clinics of Columbia-Presbyterian Medical Center and Morrisania City Hospital in a series of more than 750 cases.

There are two main groups of endocrine substances used for the male; the gonad stimulating or gonadotropic substances and the gonad substituting or androgenic substances. The gonadotropic substances are commercially available from three sources: the anterior hypophysial gonadotropins, extracts of the anterior pituitary gland of animals, chorionic gonadotropins of pregnant mare serum, and chorionic gonadotropins of human pregnancy urine. The relative effectiveness of these products depends on the total concentration of gonadotropic hormones present and the relative amounts of gametogenic and interstitial cell stimulating hormones which they contain.

Extracts of human pregnancy urine have been used extensively, because of their high concentration of interstitial cell stimulating chorionic gonadotropins, to stimulate the testes to produce androgens. The androgens, in turn, are now commercially available as testosterone propionate, in 10 mg. and 25 mg. ampules for intramuscular injection, methyl testosterone for oral administration in 10 mg. tablets and testosterone pellets to be used as implants. All three are also available as inunctions. Their action is identical to the androgens produced by the testis, namely to stimulate the accessory reproductive organs and secondary sex characteristics. As yet there is no known endocrine product capable of initiating spermatogenesis.

The physiologic action of both of these types of hormones is the induction of pubescence. The chorionic gonadotropins of human pregnancy urine act by stimulating the interstitial cells of the testes, while the androgens act through substitution for the mature testis. This, I believe, is the basis for all endocrine therapy in the prepubescent, whether it is directed

9. Bauer, J.: Common Diagnostic and Therapeutic Errors in Management of Fat Boys, M. Rec. **151:** 89 (Feb. 7) 1940. Hanssen, P.: Obesity During Growth: Clinical Study, Acta med. Scandinav. **91:** 435, 1937.

10. Kretschmer, E.: Physique and Character, translated by W. J. H. Sprott, London, K. Paul, 1925. Sheldon, W. H.; Stevens, S. S., and Tucker, W. B.: The Varieties of Human Physique, New York, Harper & Brothers, 1940.

11. Bruch, Hilde: Obesity in Relation to Puberty, J. Pediat. **19:** 365 (Sept.) 1941. Werner, S. C.: Study of Untreated "Fröhlich's Syndrome" Without Brain Tumor, J. Clin. Endocrinol. **1:** 134 (Feb.) 1941. Bauer.[9]

12. Rosenstern, J.: VIII. Ueber die körperliche Entwicklung in der Pubertät, Ergebn. d. inn. Med. u. Kinderh. **41:** 789, 1931. Kornfeld, Werner: Ueber die Habitusentwicklung in der Pubertätszeit, Wien. klin. Wchnschr. **50:** 1610 (Nov. 26) 1937.

13. Kerley, C. G., and Lorenze, E. J.: Nutritional Obesity in Children in Private Practice, J. Pediat. **19:** 241 (Aug.) 1941. Richet, C.: Nutritional Requirements of Puberty, Quart. Bull. Health Organ., League of Nations **5:** 549 (Sept.) 1936. The average diet is 900 to 1,200 calories calculated by taking two tenths of the sitting height squared [0.2 (S. H.)^2] or on the basis of the basal metabolism.

14. Start with 1 grain (0.065 Gm.) of desiccated thyroid U. S. P. daily and increase every two or three weeks by 1 grain daily until clinical improvement or toxic symptoms are evidenced. In the presence of toxic symptoms stop for one week and start again at a slightly lower dose. It must be remembered that thyroid preparations have a delayed and accumulative effect and that the various commercially available preparations differ in their calorigenic effects.

15. Kunstadter, R. H.: Experience with Benzedrine Sulfate in Management of Obesity in Children, J. Pediat. **17:** 490 (Oct.) 1940.

16. Schonfeld, W. A.: Commercially Available Newer Endocrine Products, New York State J. Med. **42:** 1538 (Aug. 15) 1942.

against sexual immaturity, eunuchoidism, inadequate or excessive growth, lack of testicular descent or merely anxiety as to genital adequacy. The treatment varies only as to the product used, dosage, duration of treatment and stage of pubescence induced (fig. 2).

PROGNOSTICATION OF SEXUAL DEVELOPMENT

In the management of the prepubescent his present genital status is of interest only as it reflects the individual's future sexual development, since the actual size of the genitalia is of physiologic significance only after pubescence. In the prepubescent one is concerned with the ability to respond to future stimulation and the probability of the anterior hypophysis to initiate this stimulation in due time.

I use various indirect methods to evaluate this prognosis, since hormone assays [17] were found to be of no aid in the prepubescent. Measurements of the penis and testes are of value to differentiate normal boys with apparently small genitalia from those with actual genital hypoplasia. It is to be remembered that the testes are normally maintained during prepubescence in a latent state by the action of minimal amounts of gonadotropic substances from the anterior hypophysis. Any disturbance of this function may cause an aplasia of the testes [3] similar to that found in primary testicular

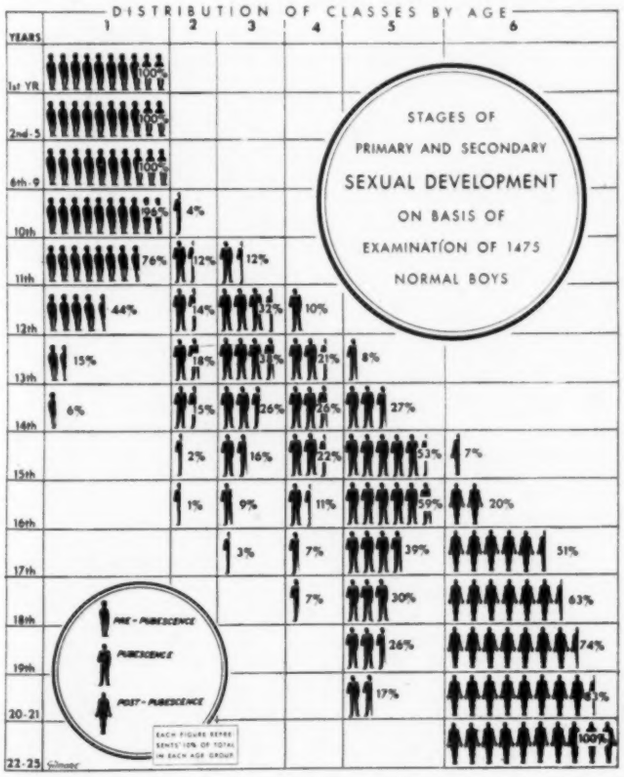


Fig. 3.—Age frequency distribution of the six stages of development and maturation. Each figure represents 10 per cent of total in each age group.

hypoplasia. Thus testing the responsiveness of the testes to large doses of chorionic gonadotropins of human pregnancy urine would help evaluate both gonadal and hypophysial factors in pubescence. This response is expressed as an increase in the circulating androgens [18] and is clinically manifested by congestion and enlargement of the penis and subsequently the prostate. This response has often been misinterpreted in the literature as a therapeutic achievement.

Usually 500 to 750 international units three times each week of a proved potent batch of chorionic gonadotropin of human pregnancy urine is adequate to stimulate the testis, but if no response is noted in two or three weeks the dose is increased to 1,500 international units three to five times each week for two or three weeks more. Evidence of response warrants the assertion that the boy has at least one normal testis and probably adequate anterior hypophysial function, so that he will have spontaneous pubescence in due time if there is no abnormal change in his status.

Fig. 4.—Appearance of a prepubertal obese boy with apparent hypoplasia of the genitalia.

CRYPTORCHISM, DELAYED PUBERTY AND EUNUCHOIDISM

In the prepubescent it is frequently difficult to differentiate bilateral cryptorchism or delayed puberty from eunuchoidism. Thus I find it necessary at times to utilize the prognosticating therapeutic test as a criterion for differential diagnosis.

Cryptorchism has been discussed so frequently in the literature [19] that I shall not review my experience except to stress the fact that a diagnosis should not be made until after thorough and repeated examinations, as illustrated in figures 6 and 7. I have often noted that in the presence of a hyperactive cremasteric reflex the testis may ascend through the open inguinal canal or under the fascia. It is important to differentiate

17. Dorfman, R. I.; Greulich, W. W., and Solomon, C. T.: Excretion of Androgenic and Estrogenic Substance in the Urine of Children, Endocrinology **21:** 741 (Nov.) 1937. Oesting, R. B., and Webster, B.: Sex Hormone Excretion of Children, ibid. **22:** 307 (March) 1938. Nathanson, I. T.; Towne, L. E., and Aub, S. C.: Normal Excretion of Sex Hormones in Children, ibid. **28:** 851 (Dec.) 1941.

18. Moore, C. R.: Gonadotropic Substances and Male Hormone Effects in the Organism, J. Urol. **42:** 1251, 1939. Sand, K., and Plum, P.: Elimination of Testicular Hormone in Urine During Treatment of Adiposogenital Dystrophy with Gonadotropic Hormone, Ugesk. f. læger **100:** 719 (June 30) 1938.

19. Counseller, V. S.: Ten Years' Experience in the Management of Cryptorchism, J. Urol. **46:** 722 (Oct.) 1941. Hamilton, J. B., and Hubert, G.: Effect of Synthetic Male Hormone Substances on Descent of Testicles in Human Cryptorchism, Proc. Soc. Exper. Biol. & Med. **39:** 4 (Oct.) 1938. Johnson, W. W.: Cryptorchism, J. A. M. A. **113:** 25 (July 1) 1939. Kunstadter, R. H.: Hormone Treatment of Cryptorchism: Eight Years' Experience, Urol. & Cutan. Rev. **45:** 81 (Feb.) 1941. Thompson, W. O., and Heckel, N. T.: Undescended Testes: Present State of Glandular Treatment, J. A. M. A. **112:** 397 (Feb. 4) 1939; Endocrine Treatment of Cryptorchism, ibid. **117:** 1953 (Dec. 6) 1941. Werner, A. A.; Kelling, Douglas; Ellersieck, Dorothy, and Johns, G. A.: Effect of Gonadotropic Extract of the Pituitary in Cryptorchism, ibid. **106:** 1541 (May 2) 1936. Zelson, C., and Steinitz, E.: Treatment of Cryptorchism with Chorionic Gonadotropic Hormones and Male Sex Hormone, J. Pediat. **17:** 315 (Sept.) 1940.

these patients with migratory cryptorchism who require no treatment, except in the presence of torsion, from those boys with an actually undescended or ectopic testis.[20] Even if both testes are undescended, the abnormal positions do not interfere with the functioning of the interstitial tissue,[21] so that pubescence develops normally. However, the seminiferous tubules usually fail to mature and degenerate with the advent of pubescence.

In eunuchoidism there is a complete aplasia of the testes so that pubescence never develops spontaneously. Once a diagnosis of eunuchoidism [22] is established an attempt should be made to differentiate patients with intracranial lesions and primary hypophysial disturbances from those with primary testicular hypoplasia as a result of a congenital defect or disturbance of testicular circulation caused by torsion or surgery.

Pubescence fails to develop in many patients with hypophysial disturbances [23] as a result of intrasellar

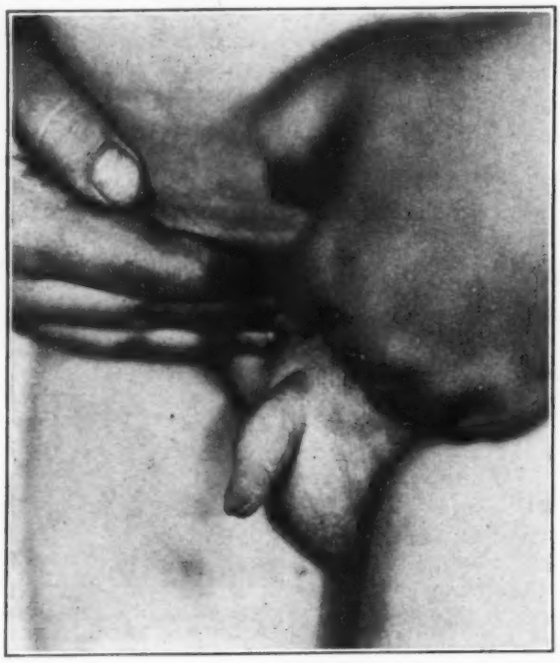


Fig. 5.—Appearance of genitalia of boy shown in figure 4. To evaluate the genitalia suprapubic fat pad is pushed back.

and of extrasellar pathologic conditions. The anterior lobe of the hypophysis is directly involved in eosinophilic tumors with gigantism, in chromophobe or basophilic adenomas or as a result of congenital aplasia of the gland, as in hypophysial dwarfism (ateliotic or Lorain-Levi). However, inflammatory or degenerative processes of the base of the brain or skull or a suprasellar neoplasm, such as a craniopharyngioma,[24] may through pressure directly on the hypophysis or through a disturbance of its circulation or neurotropic fibers also create secondary eunuchoidism.

20. Hamilton, J. B., and Hubert, G.: Differential Diagnosis of Pseudocryptorchism and True Cryptorchism, Endocrinology **21**: 644 (Sept.) 1937.

21. Rea, C. E.: Functional Capacity of the Undescended Testis, Arch. Surg. **38**: 1054 (June) 1939.

22. The term eunuchoidism is used rather than hypogonadism to imply the inability of the individual to develop pubescence spontaneously rather than refering to the size and function of his genitalia at the time of examination.

23. Bailey, Percival: Intracranial Tumors of Infancy and Childhood, Chicago, University of Chicago Press, 1939. Rasmussen, A. T.: Innervation of the Hypophysis, Endocrinology **23**: 263 (Sept.) 1938.

24. Rathke pouch tumor or hypophysial stalk tumor.

In primary eunuchoidism, the goal of treatment in children as in adults is the development of primary and secondary sex characteristics with androgens,[25] the best guide to dosage being the child's response. Start with 10 mg. of testosterone propionate by intramuscular injection three times each week or give 30 mg. of methyl testosterone daily by mouth or insert 150 mg. pellets of testosterone subcutaneously, increasing as indicated to 25 mg. of testosterone propionate hypodermically three times each week to induce pubescence. When development reaches the maximum for the individual, a maintenance dose must be established and continued through life; otherwise regression will take place.

In secondary eunuchoidism, however, the treatment should first be directed to eliminate, if possible, the primary pathologic process by means of neurologic surgery or radiation therapy. If this fails to allow pubescence to develop, or if the etiologic process cannot be eliminated, then only should androgens be used to induce pubescence.

ADIPOSOGENITAL DYSTROPHY, OR FRÖHLICH'S SYNDROME

The term Fröhlich's syndrome has been used so frequently as a diagnosis of obesity in childhood when associated with only apparent hypogonadism that its true significance has been lost.[26] The use of this term should be limited to cases of secondary eunuchoidism associated with obesity as a result of a craniopharyngioma or an inflammation or degenerative lesion involving both the hypothalamus and the hypophysis. Before labeling a boy as having Fröhlich's syndrome one should consider carefully whether he actually has adiposogenital dystrophy with a bad prognosis or merely prepuberal obesity with normal genitalia and an excellent prognosis. The treatment of Fröhlich's syndrome involves the removal of the primary pathologic process if possible and induction of pubescence with androgens. A slimming regimen is also instituted for the obesity.

PROBLEMS OF GROWTH IN HEIGHT

Although a great deal has been written about the diagnosis, pathology and treatment of the abnormalities of growth, a conclusive understanding of the problem is not available. The one approach that I consider of primary importance in the determination of the prognosis of a boy with idiopathic or hypophysial dwarfism is to evaluate his genital status.

Since the anterior lobe of the pituitary gland controls both growth and gonadal development, it is readily understood that aplasia of this gland would at times

25. Biskind, G. R.; Escamilla, R., and Lisser, H.: Implantation of Testosterone Compounds in Cases of Male Eunuchoidism, J. Clin. Endocrinol. **1**: 38 (Jan.) 1941. Eidelsberg, Joseph, and Madoff, I.: The Effectiveness of Methyl Testosterone Administered Orally, Am. J. M. Sc. **202**: 83 (July) 1941. Eidelsberg, Joseph, and Ornstein, E. A.: Observations on the Implantation of Testosterone Pellets, J. A. M. A. **117**: 1068 (Sept. 27) 1941. Hamilton, J. B.: Therapeutics of Testicular Dysfunction, ibid. **116**: 1903 (April 26) 1941. Moricard, R., and Bize, P. R.: Premières observations de développement du pénis provoqué chez l'enfant par injection d'acétate et de propionate de testostérone, Bull. Soc. de pédiat. de Paris **35**: 26 (Jan.) 1937. Tager, B. N., and Shelton, E. K.: Therapy in Male Hypogonadism: Testosterone Propionate Inunction and Methyl Testosterone Orally: Case Report, J. Clin. Endocrinol. **1**: 131 (Feb.) 1941. Turner, H. H.: Clinical Use of Synthetic Male Sex Hormone, Endocrinology **24**: 763 (June) 1939. Vest, S. A., and Barelare, Bruno, Jr.: Peroral Use of Methyl Testosterone, J. A. M. A. **117**: 1421 (Oct. 25) 1941. Vest, S. A., and Howard, J. E.: Clinical Experiments with the Use of Male Sex Hormones: I. Use of Testosterone Propionate in Hypogonadism, J. Urol. **40**: 154 (July) 1938. Webster, B.: The Treatment of Hypogonadism in the Adolescent Male, J. Pediat. **13**: 847 (Dec.) 1938.

26. Bruch, Hilde: The Fröhlich Syndrome, Am. J. Dis. Child. **58**: 1282 (Dec.) 1939. Warkany, Josef; Farber, Sidney, and Logan, M. L.: Round Table Discussion on Adiposogenital Dystrophy, J. Pediat. **19**: 854 (Dec.) 1941.

result in eunuchoidal, hypophysial dwarfism. The other forms of intracranial disorder previously discussed which might give rise to hypophysial eunuchoidism are also associated with short stature, except in cases of eosinophilic tumors, which through their excessive secretion of growth factors result in gigantism.

In the normal boy the continued secretion of hypophysial growth factors stimulates progressive growth until the onset of pubescence. At this time, probably as a result of an increase in androgens, the epiphyses receive an extra stimulus resulting in a prepuberal spurt of growth followed by fusion of the epiphyses and cessation of growth. This is associated with the further maturation of the gonads and epiphyses.

However, in primary eunuchoidism the absence of testicular development prevents fusion of the epiphyses and allows continued action of the growth factors to stimulate long bone growth, resulting in a tall eunuchoid. In cases of precocious puberty, however, the premature maturation of the gonads creates an early pubescent spurt of growth and excessive height for the child's age, which is then followed by early closure of the epiphyses and ultimate deficiency in height.

I have presented this theoretical explanation of the various problems related to idiopathic and hypophysial-gonadal dwarfism in order to create a better understanding of the rationale of treatment as I see it. When deficiency of growth is associated with eunuchoidism, as

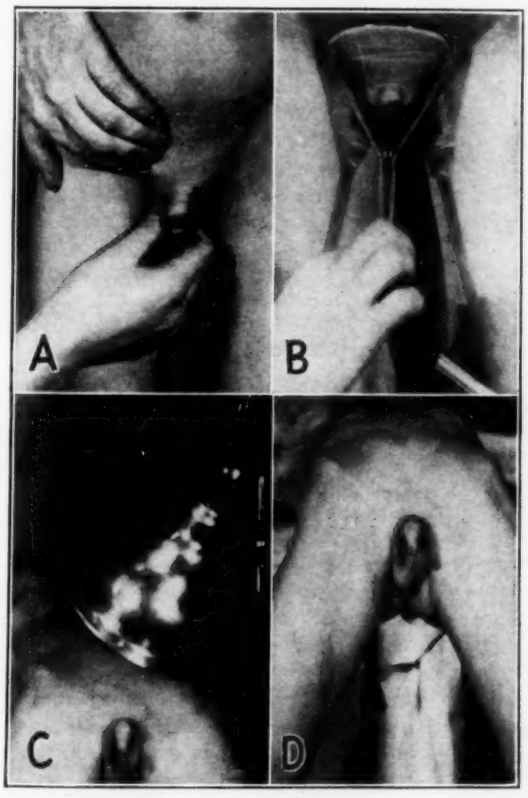


Fig. 6.—Methods of examination for position of testes. *A*, apply pressure over external inguinal ring before palpating the scrotum to prevent retraction of the testes. *B*, apply suction to stretch the scrotum and gubernaculum. *C*, apply local heat for relaxation; *D*, institute hyperextension.

proved by the fact that the boy has no genital response to large doses of chorionic gonadotropins of human pregnancy urine as previously described, the treatment is directed toward the induction of pubescence with androgens. This is usually associated with a spurt of growth.[27] However, usually deficiency in growth during prepubescence is not associated with eunuchoidism, although frequently there is a delay in the age of onset of pubescence to the upper limits of normal. In cases of short normal boys I have tried the various commercially available growth factors and found them to be of no value. I have thus reverted to the use of large doses of thyroid, adequate diet with supplementary vitamins, fresh air and exercise to stimulate the patient's maximum growth.[28]

Fig. 7.—Method of examination for position of testes in cryptorchism: the undescended vs. the migratory testis. The diagnosis undescended testis should never be made until repeated examinations fail to bring it into the scrotum.

However, in isolated instances of prepubescent boys ranging in age from 12 to 18 years, I have used large doses of androgens over a period of four to eight weeks, inducing the earliest evidence of pubescence (class 1, fig. 2) and the frequently associated spurt of growth.[29] Treatment would then be stopped for three to six months to allow regression of the genital response. This course would be repeated in the hope that a series of two or three such growth spurts would be greater than the one growth spurt which the boy would have had spontaneously. I do not generally recommend this form of treatment as it is still experimental. The danger is that the genital maturation will be carried too far, which would induce the same situation as in precocious puberty, namely a premature closure of the epiphyses and cessation of growth.[30]

ACNE

Acne occurs as a result of the increased activity of the sebaceous glands associated with hair follicle development[6] during normal pubescence. Nevertheless, it causes many pubescents a great deal of anxiety. Every endocrine substance has been used for acne but I have found none of them to be effective. Local treatment seems to be the only therapy of value. If boys are taught to use a face brush and tincture of green soap early in pubescence, severe acne can be avoided. Once it is present and secondary infection has ensued, the most effective treatment seems to be 10 per cent sulfathiazole ointment.

27. McCullagh, E. P., and Rossmiller, H. R.: Methyl Testosterone: III. Effects on Body Weight and Growth, J. Clin. Endocrinol. **1**: 507 (June) 1941. Webster, B., and Hoskins, W. H.: Influence of Androgen Therapy on Growth Rate of Hypogonadal Adolescent Boys, Proc. Soc. Exper. Biol. & Med. **45**: 72 (Oct.) 1940.

28. Meakins, J. C.: Sir Charles Clubbe Memorial Oration, Unveiling the Mystery of Growth, M. J. Australia **1**: 935 (June 19) 1937.

29. Dorff, G. B.: Chorionic Gonadotropin Effects on Height and Osseous Development in Sexually Underdeveloped Young Boys, Endocrinology **27**: 403 (Sept.) 1940. Goldzieher, M. A.: Growth and Sex Hormones, J. Clin. Endocrinol **1**: 924 (Nov.) 1941. Rubinstein, H. S., and Solomon, M. L.: Growth-Stimulating Effect of Testosterone Propionate, Proc. Soc. Exper. Biol & Med. **44**: 442 (June) 1940.

30. McCullagh, E. P., and McGurl, F. J.: The Effects of Testosterone Propionate on Epiphysial Closure, Sodium and Chloride Balance and on Sperm Counts, Endocrinology **26**: 377 (March) 1940.

GYNECOMASTIA

Normal boys frequently have some mammary tissue response during pubescence, varying from a small nodule to diffuse hypertrophy of one or both breasts, which subsides at puberty.[31] In those cases in which the enlarged breasts persist beyond puberty we have tried every form of endocrine therapy without avail. The treatment of choice for this condition is plastic surgery, except in eunuchoids, in whom androgenic therapy seems to help when the degree of gynecomastia is mild. Dr. Jerome P. Webster has perfected a mastectomy through a circumareolar incision which leaves no perceptible postoperative scar. This operation has been ideal to obviate the psychic trauma so often caused by enlarged breasts.

PSYCHOGENIC PROBLEMS

The psychologic makeup of a boy must always be taken into consideration in the management of all problems related to pubescence.[32] In using gonadotropins or androgens care should be taken not to allow the genital development to advance beyond the normal range for the boy's age and his ability to handle the ensuing emotional problems.[33] This is particularly true in the treatment of psychoneurotic and mentally retarded boys. However, the induction of pubescence in young eunuchoids obviates the many psychogenic problems associated with this condition.

If anxieties exist as to genital development, it is not enough to state that the boy's penis is normal for his age but he must accept it as being normal. I have thus at times induced early pubescence (stage 2) in perfectly normal young boys with apparent genital hypoplasia to inflate the boy's own ego if psychotherapy alone has failed.

CONCLUSION

Chorionic gonadotropins and androgens are potent drugs capable of modifying both the physical and the emotional development of the male pubescent. The judicious use of these substances requires an understanding of the physiologic mechanisms of pubescence and the action of the various substances.

A great deal of therapeutic confusion has been created in the literature by the failure to appreciate the range of normal variation of genital size, age of onset of pubescence and the characteristics of growth of the various types of body configurations (somatotypes). Many of these normal boys have been subjected to prolonged endocrine treatment with induction of pubescence, and their normal development is fallaciously attributed to endocrine therapy. An accurate evaluation of the existing status and future prognosis is essential for the proper management of the prepubescent and pubescent boy.

COMMENT

In this presentation, the developmental aspects of pubescence were stressed. Criteria were presented for the arbitrary division of development and maturation into six stages on the basis of genital measurements and associated secondary sex characteristics, and the age frequency distribution was plotted for about 1,500 boys under observation. Attention was drawn to the prolonged phase of genital latency during prepubescence and the appreciable variation in age of the onset of pubescence. These often create a problem of differentiating the normal prepubescent from the eunuchoid.

A test to prognosticate in prepubescence whether a boy will have spontaneous pubescence is based on the ability of the testes to respond to stimulation by chorionic gonadotropins of human pregnancy urine.

Induction of pubescence is the basis of nearly all endocrine therapy in this age group. The treatment varies only as to whether such endocrine products are used which stimulate the interstitial tissue of the testes to function (gonadotropins) or those which substitute for the hormones ordinarily secreted by the mature testes (androgens). The stage of pubescence to be induced also varies.

Obesity and growth should be considered in their correlation with genital development and pubescence. The criteria used differentiated in the first group the prepuberal boy with obesity from the boy with true Fröhlich syndrome and in the latter group the short normal from the hypophysial dwarf.

171 Echo Place.

31. Jung, F. T., and Shafton, A. L.: Mammary Gland in the Normal Adolescent Male, Proc. Soc. Exper. Biol. & Med. **33:** 455 (Dec.) 1935; Mastitis, Mazoplasia, Mastalgia and Gynecomastia in Normal Adolescent Males, Illinois M. J. **73:** 115 (Feb.) 1938.

32. Gordon, Alfred: Neurologic Manifestations of Puberty, J. M. Soc. New Jersey **18:** 111 (April) 1921. Wile, I. S.: Body-Mind Unity, Am. J. Orthopsychiat. **10:** 532 (July) 1940. Zachry, C. B.: Emotional Problems of Adolescence, Bull. Menninger Clin. **4:** 63 (May) 1940. Zachry, Caroline B., and Lighty, Margaret: Emotion and Conduct in Adolescence, for the Commission on Secondary School Curriculum, New York, D. Appleton-Century Company, Inc., 1940. Bize, P. R., New York, D. Appleton-Century Company, Inc., 1940.

33. Bize, P. R., and Moricard, R.: Modifications psychiques provoquées par l'injection de testostérone chez les jeunes garçons, Bull. Soc. de pédiat. de Paris **35:** 38 (Jan.) 1937. Thompson, W. O., and Heckel, N. J.: Precocious Sexual Development from an Anterior Pituitary-like Principle, J. A. M. A. **110:** 1813 (May 28) 1938.

THE HOSPITAL AND THE SYPHILIS PROBLEM IN PROSPECTIVE BLOOD DONORS

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In the United States each year a large number of persons volunteer as blood donors at the request of friends and relatives. During the present emergency the American Red Cross is collecting large quantities of blood from voluntary donors. Most of them young adults, these volunteers consider themselves in good health and free of disease. Many of them, however, are found on serologic examination by one of the standard methods to have a positive reaction for syphilis. Of 19,141 tests performed on prospective blood donors over a period of about five and one-half years at the Vanderbilt University Hospital, 3.3 per cent of the donors were found to give a positive or a doubtful serologic reaction for syphilis on one examination.[1] While a single positive or doubtful blood test is not sufficient evidence to make a diagnosis of syphilis, nevertheless the possibility that these persons may have syphilis must be considered. Many of them may go on for years without having the disease recognized unless some one notifies them of the serologic results.

This paper presents the findings of a study designed to find out what is being done about the donors who have a positive or doubtful serologic reaction for syphilis. Hospitals accepting persons as blood donors should take the responsibility of informing them if the

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1. Keller, A. E.; Kampmeier, R. H., and Frye, W. W.: Investigations of Transfusion Donors with Positive Serologic Tests for Syphilis, South. M. J. **35:** 573-576 (June) 1942.

preliminary examination indicates the presence of any disease. To determine how many hospitals did assume this responsibility and in what manner, questionnaires were sent to the superintendent of a geographically representative group of hospitals in the United States. The questionnaire prepared sought to obtain information on the following points.

1. Do you operate your own serologic laboratory for the diagnosis of syphilis?
2. If you do not operate your own serologic laboratory, where are tests performed for patients in your hospital?
3. Do you perform routine serologic tests for syphilis on all blood donors for transfusions in your hospital?
4. Do you have a procedure by which donors are notified if they have a positive reaction?
5. Who is responsible for notification of the donor?
6. Is the donor notified by interview or letter?
7. To what agency do you report positive reactions of donors?

The questionnaire was signed by the superintendent of Vanderbilt University Hospital and sent to 800 hospitals chosen from "The Transactions of the American Hospital Association for 1940."[2] In all, 603 questionnaires were returned, representing hospitals from forty-seven of the forty-eight states.

INFORMATION OBTAINED BY QUESTIONNAIRE

Serologic Laboratory Facilities According to Geographic Region.—The number and percentage of hospitals operating a serologic laboratory and testing donors for syphilis is shown in table 1. The United States was divided into eight geographic regions according to the classification of the U. S. Bureau of Census. Of the 603 hospitals, 478 operated their own serologic laboratory and 125 used public health or private laboratories. In the hospitals operating their own laboratories, 4 per cent stated that they did not test donors for syphilis. In the group of hospitals not operating a serologic laboratory, 16.1 per cent did not have a blood test for syphilis performed. Altogether 6.5 per cent stated that they were not testing blood donors for syphilis. This percentage is highest in the West North Central, West South Central and Mountain areas.

TABLE 1.—*Number and Percentage of Hospitals Operating a Serologic Laboratory and Testing Donors for Syphilis, According to Geographic Region*

Geographic Region	Total Hospitals	Operating Serologic Laboratory: Total	Operating Serologic Laboratory: Not Testing Donors for Syphilis	Not Operating Serologic Laboratory: Total	Not Operating Serologic Laboratory: Not Testing Donors for Syphilis	Percentage Not Testing Donors for Syphilis: Operating Serologic Laboratory	Percentage Not Testing Donors for Syphilis: Not Operating Serologic Laboratory	Total Percentage Not Testing Donors for Syphilis
New England and Middle Atlantic	212	158	2	54	6	1.3	11.1	3.8
East North Central	103	90	3	13	2	3.3	15.4	4.9
West North Central	69	46	4	23	7	8.7	30.4	15.9
South Atlantic	81	69	2	12	1	2.9	8.3	3.7
East South Central	35	30	3	5	0	10.0	0.0	8.6
West South Central	38	35	3	3	1	8.6	33.3	10.5
Mountain	32	22	2	10	2	9.1	20.0	12.5
Pacific	33	28	0	5	1	0.0	25.0	3.1
Total	603	478	19	125	20	4.0	16.1	6.5

Serologic Laboratory Facilities According to Size of the Hospital.—The variation according to the size of the hospital in the proportion testing and those not testing donors is presented in table 2. The percentage of hospitals not operating their own serologic laboratory and those not testing donors for syphilis is much higher in hospitals of less than 200 beds. The total not testing donors was 16.3 per cent in hospitals of 100 beds or less and 9.2 per cent in those with 100 to 199 beds.

TABLE 2.—*Number and Percentage of Hospitals Operating a Serologic Laboratory and Testing Donors for Syphilis, According to Size*

Size of Hospital (Number Beds)	Total Hospitals	Operating Serologic Laboratory: Total	Operating Serologic Laboratory: Not Testing Donors for Syphilis	Not Operating Serologic Laboratory: Total	Not Operating Serologic Laboratory: Not Testing Donors for Syphilis	Percentage Not Testing Donors for Syphilis: Operating Serologic Laboratory	Percentage Not Testing Donors for Syphilis: Not Operating Serologic Laboratory	Total Percentage Not Testing Donors for Syphilis
Less than 100	43	28	4	15	3	14.3	20.0	16.3
100-199	240	171	10	69	12	5.8	17.4	9.2
200-299	157	131	3	25	4	2.3	16.0	4.5
300-499	88	79	2	10	0	2.6	0.0	2.3
500+	75	69	0	6	1	0.0	16.6	1.3
Total	603	478	19	125	20	4.0	16.1	6.5

Only 1.3 per cent of the hospitals of 500 beds or more were not performing routine serologic tests for syphilis on blood donors. As would be expected, the percentage not testing donors was uniformly higher in all groups that did not have their own serologic laboratory than in those with a laboratory, except in the group of hospitals of 300 to 499 beds.

Serologic Laboratory Facilities According to Type of Hospital Control.—The same kind of analysis with respect to the type of administrative control shows (table 3) that the denominational hospitals had the highest percentage (10.1 per cent) not testing donors for syphilis. Only 1 of the municipal hospitals did not examine donors, and this was a hospital which operated its own serologic laboratory. The percentage not testing donors for syphilis is highest in those hospitals not operating their own serologic laboratory.

Responsibility for Notification of Positive Donors.—As pointed out previously, the hospital may require examination of prospective blood donors for syphilis, but it is also essential that they notify these donors when positive or doubtful serologic results are obtained.

The rest of this discussion deals with the methods by which the hospitals performing tests on donors fulfil their responsibility of notification.

Information regarding the responsibility for the notification of donors in hospitals examining them for syphilis is shown in tables 4 and 5. Considering the group as a whole, 9.4 per cent stated that they did not notify donors when the test gave a positive result. The private or attending physician was stated to be responsible for notifying the donor in 38.3 per cent. In about one fourth the house officer was responsible, while the pathologist or laboratory director handled the notification in approximately 14 per cent. Less than 5 per cent of the hospitals delegated the responsibility to the social service staff or to the health department. There was a fairly large proportion of hospitals which named some other agency or person responsible for notification. These included the admitting officer, the private laboratories, the superintendent's office and other hospital personnel.

2. Institutional Membership, Tr. Am. Hosp. A. **42:** 1042-1180, 1940.

When broken down according to size of hospital, table 4 shows that in hospitals of 100 beds or less and in the group of 500 beds or more the percentage which did not notify the donors having positive or doubtful serologic reactions was about 6. This percentage increased to approximately 10 in hospitals of

TABLE 3.—*Number and Percentage of Hospitals Operating a Serologic Laboratory and Testing Donors for Syphilis, According to Type of Control*

Type of Control	Total Hospitals	Operating Serologic Laboratory: Total	Operating Serologic Laboratory: Not Testing Donors for Syphilis	Not Operating Serologic Laboratory: Total	Not Operating Serologic Laboratory: Not Testing Donors for Syphilis	Percentage Not Testing Donors for Syphilis: Operating Serologic Laboratory	Percentage Not Testing Donors for Syphilis: Not Operating Serologic Laboratory	Total Percentage Not Testing Donors for Syphilis
Municipal	54	44	1	10	0	2.3	0.0	1.9
Private	289	226	6	63	8	2.7	14.3	5.2
Denominational	180	147	10	33	8	6.8	25.0	10.1
Governmental *	80	61	2	19	3	3.3	15.8	6.3
Total	603	478	19	125	20	4.0	16.1	6.5

* Other than municipal.

from 200 to 500 beds. The percentage of hospitals relying on the private or attending physician for notification decreased with the size of the hospital, being lowest in hospitals with 500 beds or more. The hospitals depending on social service personnel for notification were almost all in the group with 200 beds or more and were probably all teaching hospitals or connected with a medical school.

Table 5 shows the influence of the type of administrative control on the responsibility for notification. Almost 12 per cent of the denominational hospitals failed in any way to notify donors with a positive serologic reaction. The corresponding percentage for private hospitals was almost as high, while for governmental hospitals it dropped to 7.9 per cent. Almost

TABLE 4.—*Responsibility for Notification of Donors, According to Size of Hospital* *

Size of Hospital (Number Beds)	Number of Hospitals	Percentage Not Notifying Donors	Percentage Notifying by Private or Attending Physician	Percentage Notifying by House Officer	Percentage Notifying by Laboratory Director	Percentage Notifying by Others	Percentage Notifying by Social Service	Percentage Notifying by Health Department
Less than 100	36	5.6	75.0	8.3	0.0	11.1	0.0	2.8
100-199	218	10.6	43.1	22.9	17.0	10.6	2.8	2.3
200-299	149	9.4	38.2	28.8	17.4	12.1	5.4	4.7
300-499	85	10.6	34.1	30.6	9.4	16.5	7.0	4.7
500+	75	6.7	12.0	38.7	16.0	26.7	9.3	5.3
Total	564	9.4	38.3	26.8	14.5	13.8	4.8	3.7

* Some hospitals named more than one plan for notification of donors; therefore the percentages may add to more than 100.

all the municipal hospitals examining donors notified them in some way, only 3.8 per cent failing to do so. It is seen that 54 per cent of the denominational and 39.4 per cent of the private hospitals placed the responsibility for notification in the hands of the private or attending physician. There was not a great deal of variation with type of control in the percentage of hospitals using the house officers to notify donors. The same is true of hospitals utilizing the pathologist or laboratory director or the health department. In the municipal hospitals 13.2 per cent stated that the social service personnel notified donors.

Methods Used to Notify Positive Donors.—Tables 6 and 7 show the methods used to notify donors with positive reactions. There was no definite plan or system for notifying them in 12.5 per cent of the hospitals. Approximately half of the hospitals stated that these donors were informed of the serologic findings by personal interview. The private or attending physician was listed as the means of notification in 2[illegible].5 per cent of the hospitals, which was interpreted as meaning that the physician was left with the entire responsibility. Only 7.8 per cent notified by letter and 7.6 per cent by letter and interview. The group using other methods included those stating that the donor was notified by telephone or by other members of the family.

The effect of the size of the hospital on the method of notification is shown in table 6. The percentage of hospitals having no method of notifying donors decreased with increasing size of the hospital, with the

TABLE 5.—*Responsibility for Notification of Donors, According to Type of Hospital Control* *

Type of Control	Number of Hospitals	Percentage Not Notifying Donors	Percentage Notifying by Private or Attending Physician	Percentage Notifying by House Officer	Percentage Notifying by Laboratory Director	Percentage Notifying by Others	Percentage Notifying by Social Service	Percentage Notifying by Health Department
Municipal	53	3.8	15.1	26.4	13.2	30.2	13.2	5.7
Private	274	9.5	39.4	27.4	16.8	11.7	5.8	3.3
Denominational	161	11.8	54.0	21.7	11.8	8.1	0.0	3.7
Governmental †	76	7.9	17.1	35.5	14.5	10.5	5.3	3.9
Total	564	9.4	38.3	26.8	14.5	13.8	4.8	3.7

* Some hospitals named more than one plan for notification of donors; therefore the percentages may add to more than 100.
† Other than municipal.

exception of hospitals with 300 to 499 beds. Smaller hospitals, or those with less than 200 beds, leave the problem of notification in the hands of the private physician, while larger hospitals seem to rely more on the interview or letter or both as a means of notification of donors.

Table 7 shows the methods used to notify donors according to the type of administrative control. The private and denominational hospitals show the highest percentage having no system for notification of donors. When they do have a system they favor the interview as the method of notification, although denominational hospitals depend somewhat more on the private or attending physician.

The municipal and governmental hospitals use the same methods for notifying donors. Only about 7 per cent had no method for notification, and approximately one half of this group of hospitals notify by personal interview. Since the number of private patients are fewer in this group of hospitals, the private or attending physician was listed as the means of notification in only 5.8 per cent of the municipal and 13.8 per cent of the governmental hospitals. In 25 per cent of the municipal hospitals letters were used and in 11.5 per cent both letter and interview.

COMMENT

This study shows that 6.5 per cent of the 603 hospitals from which replies to the questionnaire were received did not test blood donors for syphiiis before their blood was used. Of the hospitals testing donors for syphilis 12.5 per cent had no method for notifying these donors when they were found to have a positive or doubtful serologic reaction. Of the 603 hospitals, then, 16.2 per cent either did not examine donors for syphilis or did not notify them when the serologic test was found to be positive.

It is impossible to determine how many persons are examined each year as prospective blood donors. There is no doubt that several thousand of these donors will have a positive reaction suggesting the presence of syphilis. In a large proportion of cases a blood donor found to have syphilis is not aware of the infection. If these positive donors are not informed of the results of the laboratory tests and if the significance is not explained to them, they may transmit the disease to others or late manifestations of the disease may develop which could have been prevented by treatment. Hospitals, therefore, should develop some system for notification and follow-up of each donor found to have a positive serologic reaction for syphilis.

That most hospitals would attempt to correct this situation if it were called to their attention would seem to be borne out by some of the letters which were returned with the questionnaires. The following letter was received from a hospital connected with a large medical school:

> Your questionnaire called to our attention a very definite deficiency in our practice; namely, that we have not been informing blood donors of the findings in connection with Wassermann tests that were made. This deficiency has now been corrected and the member of the house staff who withdraws the blood sample has been made responsible for informing the donor of the result of the Wassermann examination, particularly in cases where findings are positive, and of advising them concerning treatment.

Another letter states:

> At the time we received your inquiry we did not do serological tests on donors, but since then we have made it a standard practice.

TABLE 6.—*Methods Used to Notify Positive Donors, According to Size of Hospital*

Size of Hospital (Number Beds)	Number of Hospitals	Percentage Having No Method of Notifying Donors	Percentage Notifying by Interview	Percentage Notifying by Private or Attending Physician	Percentage Notifying by Letter	Percentage Notifying by Interview and Letter	Percentage Notifying by Other Methods	Total Percentage
Less than 100	36	20.0	25.7	45.7	5.7	2.9	0.0	100.0
100-199	218	13.2	46.8	32.2	2.4	4.7	0.45	100.0
200-299	149	10.3	55.2	17.9	7.6	6.2	2.8	100.0
300-499	85	16.7	40.5	19.0	9.5	11.9	2.4	100.0
500+	75	6.6	50.0	4.1	23.0	14.9	1.4	100.0
Total	564	12.5	47.1	23.5	7.8	7.6	1.5	100.0

Such letters indicate steps in the right direction. In order, however, for hospitals to have a successful system for notification of donors, the problem must be handled by one person. This person should be a permanent member of the hospital staff and all serologic tests for syphilis on blood donors should be reported to the person responsible for notification.

It has been our experience that a plan which depends on the house staff or the private physician is not satisfactory. A more definite system for notification of donors with positive serologic reactions is necessary, as emphasized in a study of serologic reactions for syphilis in blood donors made at Vanderbilt University

TABLE 7.—*Methods Used to Notify Positive Donors, According to Type of Hospital Control*

Type of Hospital Control	Number of Hospitals	Percentage Having No Method of Notifying Donors	Percentage Notifying by Interview	Percentage Notifying by Private or Attending Physician	Percentage Notifying by Letter	Percentage Notifying by Interview and Letter	Percentage Notifying by Other Methods	Total Percentage
Municipal	53	7.7	50.0	5.8	25.0	11.5	0.0	100.0
Private	274	15.3	49.6	20.2	6.4	7.8	0.7	100.0
Denominational	161	12.1	38.5	40.4	1.3	4.5	3.2	100.0
Governmental *	76	6.8	54.0	12.2	14.8	10.8	1.4	100.0
Total	564	12.5	47.1	23.5	7.8	7.6	1.5	100.0

* Other than municipal.

Hospital in 1937.[3] In July of that year a plan for notification was developed whereby persons who volunteered as blood donors were asked to specify whether or not they wished to be informed of the results of the serologic test in the event of a positive reaction. At the time the specimen of blood was obtained the donor was asked to sign a printed form indicating whether or not he wished to be notified by personal interview or by letter. Duplicate forms were to be made out by the house officer who drew the blood from each donor. This plan failed, since the house officer, owing to lack of time and interest, soon neglected to fill out the forms. During the two and one-half years that this plan was used the house officers were given the entire responsibility for notification, but only very few donors were informed of the result of the test unless a special effort was made on their part to get in touch with the same house officer who drew the blood. Since July 1940 one of us has taken the responsibility for notification of all donors who are found to have a positive or a doubtful serologic reaction for syphilis. All donors are notified by letter or by personal interview. If there is no response to the letter, a visit is made and the need for another blood test is explained to the donor. If the second test gives a positive reaction, the person is referred to his family physician or to a clinic for final diagnosis and treatment. With this plan much better results were obtained.

If hospitals do not have a system for notification of donors, they should be encouraged to report all donors found to have a positive or doubtful reaction as syphilis suspects to the health department. The health department should assist in getting donors with a positive serologic reaction under treatment in the same way in which they are now assisting local draft boards to get a second blood test on registrants found on first examination to have a positive or doubtful reaction for syphilis.

It is felt that if the hospitals of the country will develop a satisfactory system of notification, they will not only contribute to the syphilis control program but

3. Keller, A. E., and Leathers, W. S.: Serologic Reactions for Syphilis in Blood Transfusion Donors, Ven. Dis. Inform. **20**: 5-9 (Jan.) 1939.

they will render a definite service to a large number of persons who are unaware of the fact that they have syphilis.

SUMMARY

1. A questionnaire was sent to 800 hospitals to determine whether or not blood donors found to have a positive or doubtful serologic reaction for syphilis were notified of the results of the test and how they were notified. Replies were received from 603 hospitals.

2. Of the 603 hospitals 6.5 per cent did not test blood donors for syphilis before their blood was used.

3. Of the hospitals testing donors for syphilis, 12.5 per cent had no method for notification of the donors found to have a positive or doubtful serologic test.

4. In all 16.2 per cent of the hospitals either did not examine donors for syphilis or did not notify them when the serologic test was found to be positive.

5. The person or agency responsible for notifying donors with a positive serologic reaction and the method of notification varies according to the size of the hospital and the type of administrative control.

6. The findings indicate the need in many hospitals for a more definite system whereby prospective blood donors found to have a positive or a doubtful serologic reaction for syphilis may be notified of the result of the test.

ABSTRACT OF DISCUSSION

DR. HAVEN EMERSON, New York: When we are looking around for ways of bringing this problem, syphilis, to people's attention, the blood donor system must be recognized as a matter of considerable importance, and here we have an instance of the way it can be used, and well used, with good results. I hope we can get attention for this by the American Hospital Association and other professional bodies concerned with blood banks and well controlled blood donor systems.

DR. JOSEPH W. MOUNTIN, Washington, D. C.: It is astounding that any hospital should accept donors without a blood test. I am surprised to find that a fair proportion are doing so. That prompts me to ask several questions in respect to this group. You have some six hundred hospitals in the group. I am wondering how representative they are of the hospitals of the United States. Do you think that you got the hospitals which showed the best performance? Would the hospitals whose performance was not so good be the ones who would be likely to fail to send back your questionnaire? Have you any information as to what was done with respect to persons who showed positive reactions? Did the hospitals continue to use them as donors, or were they rejected? I noticed that they were not notified of having the infection, or 10 per cent of them were not. I noticed too that you classified hospitals as follows, and I quote: "municipal, other governmental, private, denominational"—and that does not exactly conform to the classification used in the Hospital Register, for example, of the American Medical Association, which uses the description "governmental, nonprofit and proprietary." Is the term "private" as herein used intended to be synonymous with "nonprofit," and is "denominational" synonymous with "religious"? If so, what becomes of the other group of voluntary hospitals which do not fall within the categories "private" or "denominational"? Is there any legal responsibility involved in the failure of the hospital to take what would seem to be reasonable precautions against the transfer of infections?

DR. EMERSON: Under the blood betterment, it would be impossible to have any blood donor that did not have the blood test before blood was taken.

DR. WILLIAM C. WOODWARD, Washington, D. C.: The law, I believe, very generally requires any one who finds that a person who he examines or treats is suffering from syphilis to report that fact to the proper authorities. If such a report states the name of the syphilitic person, surely those authorities get in touch with him, at least unless they are assured that he is under treatment by some licensed practitioner who has assumed responsibility for the case. If the report describes the syphilitic person only by number—as I believe is sometimes permissible—then he may remain officially anonymous, but only so long as he is known to be under treatment. How is it possible, then, for a blood donor who has been found to have syphilis to remain in ignorance of that fact or to avoid the inconveniences usually associated with it?

DR. H. R. O'BRIEN, Hartford, Conn.: Is there not another provision in many states requiring approved laboratories to report to the health department positive Wassermann reactions?

DR. EMERSON: If the state system has an approved laboratory.

DR. O'BRIEN: In how many states does that arrangement obtain?

DR. WILLIAM W. FRYE, Nashville, Tenn.: These problems were brought to our attention several years ago, and the present study was undertaken to determine how other hospitals were handling prospective blood donors found to have a positive blood test for syphilis. We too were surprised to find from the survey that there are some hospitals in the United States using blood donors without running a serologic test for syphilis. This question was answered, in many instances, "We do not do blood tests on donors used in this hospital." This report is based on a geographically representative sample of hospitals taken from the Transactions of the American Hospital Association for 1940. The type of hospital control, such as "denominational," is the classification used by the American Hospital Association. As to the rejection of donors, the donor is often told that his blood is "no good" or his "blood is bad" or "it wont match." When donors are asked about what they were told they think that all these statements mean that the blood will not match, and they have no idea that the single test indicated that they have syphilis. With regard to legal responsibility, certainly a hospital should be responsible for notifying the person. There are a few states which have laws, New York State for example, requiring that all laboratories report positive blood tests to the health department. With regard to Dr. Woodward's question, the reporting of positive bloods to the government agencies does not solve the donor problem. In most cases the prospective donor is seen only once. If his blood test is doubtful or positive on one examination, this is not sufficient evidence to make a diagnosis of syphilis; and unless the donor is brought back and checked, this is not reported as a case of syphilis. We have found that in many cases, in our own hospital, the donor had a positive blood, and the intern on the case was the only one who knew the result of the test. The donor was never called back and the intern did not report the case, as he had only a single blood test, which is not sufficient evidence to make a diagnosis of syphilis. Unless some one in the hospital assumes the responsibility for recheck and notification, the donor with the positive test never knows that he may have syphilis. In reporting positive donors to the health department, the case is reported from a hospital and it is assumed that the patient is under treatment. With such a method the prospective donor may be reported as a case of syphilis and yet he has never been informed of the fact that he has syphilis. No one has taken the responsibility for getting another blood test or for explaining to the donor the importance of a complete examination and treatment if a definite diagnosis of syphilis is made.

London Fogs.—Owens has studied the nature of London fogs and found that the amount of suspended solid particles is proportional to the fog density. He found 1 mg. of solid material per cubic meter of air on a clear day, as contrasted with 5 mg. per cubic meter in a dense fog. The latter figure represents 195 tons of suspended solid material over the area of London. He found the diameter of the solid particles to vary between 0.00013 and 0.00026 mm. in diameter. Water to a depth of 0.0014 mm. was condensed on the surface of these solid particles. The number of particles present in such polluted air may rise to more than 50,000 per cubic centimeter. Under these conditions about 500 billion particles per day would be inhaled by an adult person.—West, Edward S.: Physical Chemistry for Students of Biochemistry and Medicine, New York, Macmillan Company, 1942.

THE HAZARD OF PARALDEHYDE ADMINISTRATION

CLINICAL AND LABORATORY STUDIES

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A number of fatalities following paraldehyde administration have been reported which invariably have been attributed to an idiosyncrasy. However, analysis of reported autopsy findings, observations in the clinic and laboratory investigations on experimental animals lead to the conclusion that pathologic changes following the intravenous administration of paraldehyde are so definite that its use in this manner is not warranted.

Paraldehyde has gained in popularity because of its convenient applicability to produce unconsciousness. It has been administered orally, rectally and intravenously. The doses recommended have been variable. Indeed there are reports of human tolerance of massive doses. As much as 100 cc. has been ingested with recovery.[1] For rectal instillation 30 cc. has been recommended in the average adult.[2] Intravenously the injection of fractional doses of 2 to 3 cc. until the desired effect is obtained [3] has been advocated. Undoubtedly, rapidity of absorption is a great factor, since deaths have occurred following the ingestion of 25 cc.[4] and the rectal injection of 12 cc.[5]

Paraldehyde was first used in Italy by Cervello [6] in 1884 and in England by Strahan.[7] The first report of a death attributable to this drug appeared in 1890.[4] Six teaspoons had been given, by mouth, to an adult delirious typhoid patient. Five minutes later the patient "fell into an unconscious state" and died four hours later from "failure of the heart's action." Since this early publication there have been numerous reports of instances of so-called paraldehyde poisoning or idiosyncrasy to paraldehyde. Only a few of the reports which included autopsy findings will be reviewed briefly.

MacFall [8] reported the death of a man aged 41 who had ingested about 75 cc. of paraldehyde. Autopsy revealed severe congestion of both lungs.

McDougall and Wyllie [9] reported the death of a psychotic woman aged 44 who drank 4 ounces (120 cc.) of paraldehyde. In a few minutes she was in profound coma and showed signs of cardiac failure as evidenced by pallor and rapid, thready pulse. Despite restorative treatment with oxygen, she died fifty hours later. At autopsy both lungs were deeply congested and there was considerable mucus in the trachea.

Kotz, Roth and Ryon [10] reported the death of a woman aged 31 who was given 31 cc. of paraldehyde rectally for obstetric analgesia. She was a healthy woman and had received no other sedative medication. Ten minutes after administration of the paraldehyde the patient was in deep sleep, the respiratory rate having incerased from 20 to 40 a minute and the heart rate from 90 to 120. A half hour later she was in coma with cyanosis, labored and rapid respirations and a rapid, irregular pulse. Three hours later auscultation disclosed a loud blowing murmur over the tricuspid area indicative of failure of the right side of the heart. The blood pressure diminished from 148 systolic and 98 diastolic to 118/58 millimeters of mercury. Despite treatment for heart failure (oxygen, withdrawal of 250 cc. of blood, digifoline intravenously and 100 cc. of 25 per cent dextrose intravenously), pulmonary edema developed and the patient died eight hours after the administration of paralhehyde. Findings at autopsy revealed hypostatic congestion with edema of both lungs and severe dilatation of the right side of the heart.

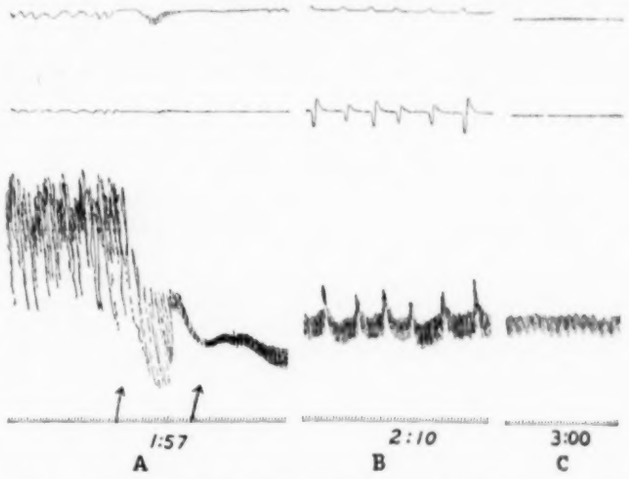

Fig. 1.—Records of dog weighing 10 Kg. from above downward represent thoracic respiratory movements, abdominal respiratory movements, arterial blood pressure and time at intervals of one second. At *A*, 5 cc. of paraldehyde was injected intravenously in twenty-five seconds. Prior to the injection the control respiratory rate was 14 a minute and the arterial blood pressure (under local anesthesia) was 180 systolic and 100 diastolic. During the course of the injection a period of apnea was observed while the blood pressure fell to 110/40 and soon reached a level at 60/48. In strip *B*, thirteen minutes after the injection, the animal was in second plane surgical anesthesia. The respiratory rate had increased to 120 a minute with very shallow excursions. The abdominal respiratory record showed definite accessory abdominal contractions which occurred every eight or nine seconds. The arterial blood pressure was 80/60. In strip *C*, fifty minutes later, the animal had regained consciousness and reacted to all forms of stimuli, but respirations remained rapid (over 200 a minute) and shallow. Arterial blood pressure still remained at 80/60 (a fall of 55 per cent from the control reading). This animal died eighteen hours later of acute pulmonary edema with dilatation of the right side of the heart.

A case analogous to the one just cited was reported by Shoor.[5] Twelve cc. of paraldehyde in 6 cc. of benzyl alcohol and 30 cc. of isotonic solution of sodium chloride was administered rectally to a healthy obstetric patient aged 21. Three and one-half hours later the patient was cyanotic and comatose. Respirations were 48 a minute and labored, the pulse rate was 148 a minute and irregular and the arterial blood pressure had fallen from 130/90 to 96/56. Despite oxygen therapy and cardiac supportive measures, pulmonary edema ensued and the patient died twenty-one and one-half hours after the administration of paraldehyde. Autopsy revealed acute pulmonary congestion and edema.

From the Division of Surgery, Department of Anesthesia, New York University College of Medicine.

Read before the Section on Anesthesiology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1942.

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REPORTS OF CASES

Two fatalities are here reported:

CASE 1.—A man aged 58 was to undergo an endothermic resection of a carcinoma of the cheek and excision of the cervical glands. Several months previously a similar resection had been performed during chloroform anesthesia. The use of intravenous paraldehyde was proposed for the second operation because of the supposedly greater safety of the latter drug. Morphine sulfate ⅙ grain (0.01 Gm.) and scopolamine hydrobromide 1/150 grain (0.0004 Gm.) was administered subcutaneously at 1:30 p. m. At 2:45, just prior to anesthetization, the patient's arterial blood pressure was 140/90, pulse rate 82 a minute and respiratory rate 18 a minute. At 2:57 intravenous injection of paraldehyde was started. Twenty-three cc. was injected in nine minutes when the patient appeared to be in second plane anesthesia but operation could not be started because of coughing. Five cc. more was injected in thirty seconds. The arterial blood pressure had fallen to 100/80 with a pulse rate of 100 a minute. The patient, however, was not sufficiently anesthetized and another 5 cc. was injected in thirty seconds. This was further complicated by attacks of coughing, so that additional injections of 4 cc. of paraldehyde in thirty seconds, followed by 3 cc. in twenty seconds were administered. This made a total of 35 cc. of paraldehyde before the patient appeared ready for operation. At this time the patient's blood pressure was still 100/80, the pulse rate 96 a minute and the respiratory rate 56 a minute. An endotracheal tube was passed by the nasal route to assure a patent airway, and operation was begun and completed in thirty-five minutes. At this point the patient seemed to be recovering from his anesthesia, as evidenced by roving eyeballs, swallowing, coughing and responding to supraorbital pressure. The patient was nevertheless returned to the ward with the nasotracheal tube in place. The tube was removed at 5:40 when the patient had regained his reflexes and maintained a patent airway. The pulse rate was then 114 a minute and respirations were 36 a minute. At 7:10 the patient became cyanotic. Oxygen by nasal catheter and an intravenous infusion of 1,000 cc. of 5 per cent dextrose in isotonic solution of sodium chloride were started. The patient died at 8:45 despite artificial respiration with oxygen for the last twenty minutes. Permission for a postmortem examination was not obtained.

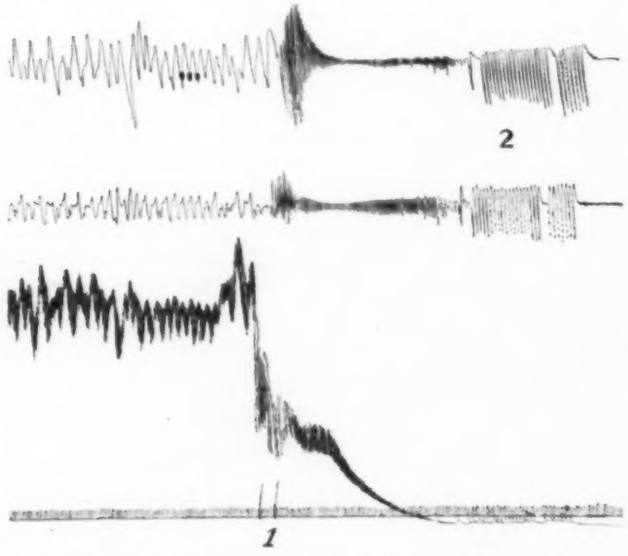

Fig. 2.—Records of dog weighing 14 Kg. from above downward represent thoracic respiratory movements, abdominal respiratory movements, arterial blood pressure and time at intervals of one second. At 1, 7 cc. of paraldehyde was injected intravenously. The respiratory rate increased from 16 to 72 a minute while the arterial blood pressure, previously recorded under local anesthesia, fell abruptly to the zero level. Artificial respiration immediately instituted at 2 was valueless.

CASE 2.—An obese white man aged 38 presented signs of acute peritonitis. His condition was complicated by delirium tremens. Celiotomy under ether anesthesia disclosed pancreatitis. Eighteen hours after the operation signs of alcoholic encephalopathy developed characterized by irrationality and delirium tremens. Morphine was ineffective as a sedative. Paraldehyde was then ordered, 15 cc. to be administered by mouth every six hours. The first two doses had little or no effect in quieting the patient. A third dose was given in the evening, but restraint was still necessary. Three hours after the third dose of paraldehyde the patient was found dead in bed. At autopsy severe pulmonary congestion was observed.

Fig. 3.—Showing pulmonary hemorrhages in the right side of the heart.

In the reported fatalities following administration of paraldehyde death occurred by the development of acute failure of the right side of the heart and autopsy showed pulmonary congestion with edema and dilatation of the right side of the heart. That these pathologic complications were not a coincidence was borne out by studies on experimental animals.

EXPERIMENTATION

To evaluate the effects of intravenous paralydehyde on the cardiovascular and respiratory systems, 28 dogs, 36 cats and 24 rabbits were used.

In the dogs, control arterial blood pressure readings were recorded by cannulating a femoral artery under local anesthesia with 2 per cent procaine hydrochloride. Control respiratory movements were obtained by applying pneumographs to register thoracic and abdominal movements. No sedative or other medication was used. Paraldehyde,[11] 0.5 cc. per kilogram, was then administered intravenously at the rate of 1 cc. in five seconds. Under these conditions, 16 of the 24 dogs displayed general anesthesia lasting seventeen to sixty-four minutes (group 1), while the other 8 died within five minutes (group 2).

In group 1, the same sequence of events affecting the cardiovascular and respiratory systems was repeatedly reproduced and is illustrated in figure 1. The arterial blood pressure fell abruptly during the injection of paraldehyde to attain a level averaging a reduction of more than 50 per cent of the control level. This low level was maintained during the anesthetic phase and remained after the animal regained consciousness. The heart rate showed a compensating tachycardia from 80 to more than 200 a minute. Respiratory changes were likewise consistent. Immediately after injection of paraldehyde there was apnea for several seconds. This was followed by rapid, shallow respira-

11. The paraldehyde used was obtained from the Bellevue Hospital Pharmacy from the supply used routinely for clinical patients.

tions, the rate increasing from 14 to 20 to as much as 200 a minute while the minute volume decreased sharply. Accessory muscles of respiration were used often, especially the abdominal muscles. Coughing occurred frequently. Cyanosis, which became progressively more intense, was noted; determinations of the oxygen of the arterial blood showed a reduction from 17.3 to 8.8 volumes per cent. The majority of the animals in this group (11 out of 16) died six to twenty-four hours after anesthesia. Autopsy revealed acute pulmonary edema with multiple areas of gross hemorrhage in both lungs, dilatation of the right side of the heart and congestion with edema of all the viscera.

The remaining 5 animals in this group survived but looked weak and had anorexia. Three of them died within two weeks, and autopsy revealed multiple pulmonary hemorrhage.

In the second group of 8 dogs which died within five minutes after paraldehyde injection the respirations rapidly increased in rate, while the arterial blood pressure fell precipitiously (fig. 2). Respiratory and circulatory collapse appeared simultaneously. An attempt at immediate artificial respiration by rhythmic pulmonary inflation of oxygen through a tube passed into the trachea was of no avail. Autopsy revealed massive diffuse pulmonary hemorrhages and dilatation of the right side of the heart distending the pericardial sac. To obtain a better knowledge of what occurred, paraldehyde was injected intravenously in a group of 6 dogs and 6 cats whose chests were opened in the midline so as to expose the heart and lungs. This was done under light anesthesia with soluble pentobarbital and artificial respiration maintained by rhythmic inflation of air through a tracheal tube.

Kodachrome motion pictures were made in two of the experiments. It was observed that immediately following the injection of paraldehyde the lungs suddenly blanched while the right side of the heart, both the ventricle and the auricle, dilated. The left ventricle contracted forcefully for a short time while the lungs

Fig. 4.—Dilatation of the right side of the heart.

began to be mottled by areas of hemorrhage which increased steadily in size. After three to five minutes cardiac arrest supervened. Figure 3 shows the pulmonary hemorrhages and figure 4 the cardiac dilatation observed in one experiment. Figure 5 is a graphic representation of the cardiac dilatation obtained by means of a myocardiograph.

To obviate a species susceptibility, similar experiments were repeated on 36 cats and 24 rabbits with identical results. It was further determined that the minimum anesthetic dose (smallest dose that produced anesthesia) when paralydehyde was administered intravenously was 0.3 cc. per kilogram of body weight in

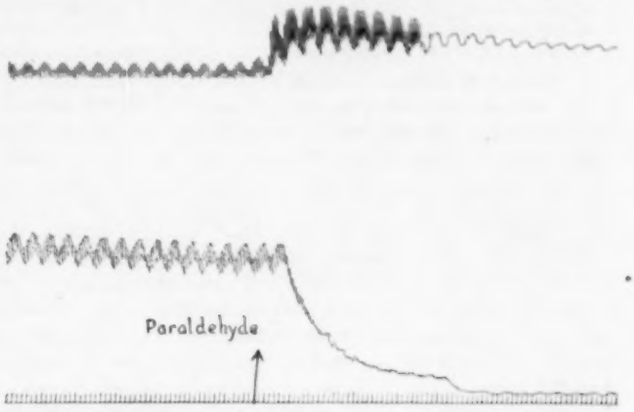

Fig. 5.—Upper record of myocardiogram of dog weighing 12 Kg. Middle record, arterial blood pressure. Bottom record, the time at intervals of one second. Following the injection of 6 cc. of paraldehyde intravenously the myocardiogram showed definite cardiac dilatation.

all 3 animal species. The minimum lethal dose (dose at which 50 per cent of the animals died) was found to be 0.45 cc. per kilogram in cats and rabbits and 0.50 cc. per kilogram in dogs. These figures represent a low margin of safety.

SUMMARY

Paraldehyde administered intravenously is not as safe as is generally believed.

Autopsy findings in reported clinical fatalities are similar to those reproduced in experimental animals, namely dilatation of the right side of the heart with pulmonary hemorrhages and edema.

Clinically, these fatal complications are preceded by signs of acute failure of the right side of the heart.

Experimentally, the rapid development of cardiac dilatation and pulmonary hemorrhages can be observed in the open chest following administration of intravenous paraldehyde.

477 First Avenue.

ABSTRACT OF DISCUSSION

DR. RALPH T. KNIGHT, Minneapolis: Dr. Burstein has done a service in collecting these case reports of others, presenting the informative details of the 2 cases which were available to him and following them through with corroborating animal experimental evidence of the mechanism of death by paraldehyde. His finding of the extremely low margin of safety between the minimum anesthetic dose and the minimum lethal dose is especially noteworthy and should be well considered by any one who contemplates using this drug. Probably few members of this section have had occasion to use paraldehyde. It was used by a good many in the latter part of the last century and in very recent years we have been reminded of its availability and serviceability. The uses for which it has been especially advocated are, first, the control of alcoholic and psychotic confusion and delirium states and, second, the control of anxiety and distress during the first stage of labor. These uses call for an amnesic or hypnotic rather than an anesthetic. Possibly, if the clinical employment of paraldehyde is confined to this mild effect and larger doses with their more potent effects are meticulously avoided, the margin of safety may be much wider. Still one must heed the warning voiced by Dr. Burstein. Obstetric analgesia and anesthesia are still relatively much less satisfactory than our present methods and

results in surgical anesthesia. In their desire to improve their obstetric service many may still be tempted to explore the clinical possibilities of paraldehyde. In public hospitals, especially with limited budgets for more expensive drugs, this may be true. My only use of paraldehyde has been in the Minneapolis General Hospital, where it has been employed only for control of unmanageable alcoholic and psychotic patients on their admission. It has then been administered intravenously in doses of 2 to 8 cc., just sufficient in each case to obtain relative quietness. I believe that no more than 10 cc. has ever been injected at this hospital. We have had no fatalities, but in the last two years other resources have displaced this method. The impressive warning is that the pathologic condition which causes death, as shown by Dr. Burstein, develops not necessarily at once but during a period of time following anesthesia, and there is no criterion while we are administering the drug to tell us whether or not we still have given too little to cause the fatal changes. If one employs it one must do so after weighing the possibilities and deciding that, under the individual circumstances, it is still the most serviceable choice. It is a little difficult to think up illustrative instances in which this would be true. I should like to ask Dr. Burstein whether he believes that the initial toxic effect is on the capillaries and tissues in both the lungs and the heart or whether the pathologic condition in either one is secondary to the failure of free circulation of blood through the other.

DR. C. L. BURSTEIN, New York: In answer to the question of Dr. Knight on the toxic effect, whether it is on the capillaries or on the tissue itself, I have done several experiments, as yet unpublished, which lead me to believe that paraldehyde is a capillary poison. I have also done other experiments, such as injecting paraldehyde, not intravenously, but into the left ventricle, and in those experiments no pulmonary hemorrhages were observed but the animals died promptly, probably from some cerebral accident.

THE USE OF PROGESTERONE IN THE TREATMENT OF POSTPARTUM PSYCHOSIS

HARRY J. SCHMIDT, M.D.
CONVENT, LA.

A review of the literature shows that this condition occurs in every 400 to 1,000 deliveries. The variation of the figures is due to the fact that there is no line of demarcation between extreme nervousness with minor changes and a definite psychosis. Statistics show that postpartum psychosis constitutes about 10 per cent of the female admissions to the psychopathic hospitals.

The duration of the condition is from several weeks to eight months, the prognosis for ultimate recovery in the true postpartum psychosis being good.

The cause of this psychosis is as yet a matter of speculation and theory. No common findings are noted among the case reports. Psychogenic factors are not always present. Infection, shock and difficult labors are not constantly found. As a rule there is no evidence of toxemia. The literature is confusing and contradictory, indicating that the real cause is as yet unknown. The definite predisposing factor is delivery.

The nature of the psychosis indicates that the condition is definitely a clinical entity. No record was found of a postpartum psychotic patient ever developing a psychosis subsequently from any of the numerous stresses and strains of a lifetime. The favorable prognosis for ultimate recovery and the common recurrence of the psychosis following subsequent pregnancies indicate that the condition is probably due to some disturbance of a physiologic nature resulting from the sudden termination of pregnancy. Complete recovery without specific therapy in a period of weeks or months tends to prove definitely that some readjustment is accomplished with time.

The symptom complex of the psychosis varies with each person, the whole gamut of psychiatric illnesses being observed in these patients. The detailed classification of the psychiatrist is based solely on the behavior of the individual and is purely symptomatic. It has no important bearing on either the cause or the treatment.

REPORT OF CASE

A white woman aged 21 was seen throughout the pregnancy. It was noted that she was unusually quiet and calm, especially for a first pregnancy. The patient was healthy, well adjusted to married life and very desirous of a child. She was advised to go to a hospital for delivery because the pelvic measurements were slightly under normal, although no grave difficulties were expected. She was delivered in a state hospital by low forceps with episiotomy. The labor was normal and of ten hours' duration. There were no complications of the puerperium, and the patient was discharged on the fifth day.

Two days after her return home she developed noticeable nervousness, suffered from insomnia and eventually became hysterical. The condition became progressively worse, and the patient developed a definite psychosis. She was readmitted to the same hospital to a gynecologic service. A pelvic examination showed no abnormal findings, and she was discharged within twelve hours.

The following day she became irrational, had convulsive seizures and was admitted to the neuropsychiatric ward. The case was completely worked up with a diagnosis of postpartum psychosis-schizophrenia.

The physical and neurologic examinations disclosed no abnormalities. The essential laboratory findings showed nothing of importance. The family history revealed that a married sister became somewhat nervous after pregnancy. The mental status of the patient was recorded as follows: "Behavior: general excitement, constant stream of talk. Flight of ideas, mostly about religion. Mood: sadness. Conduct: feeling of guilt; thinks she is going to Heaven. Sensorium: disoriented as to time and place." It was necessary to restrain the patient; she refused to eat, and nourishment was given through a tube. Infusions were also used. In a febrile period the temperature went as high as 103 F., the cause of which could not be determined. During this time the patient had a profuse uterine hemorrhage which was almost fatal. Several transfusions were given. The patient eventually recovered without specific treatment and was discharged as apparently normal after a stay of five weeks in the hospital.

Two weeks after her return home she again developed the psychosis. On the fifth day she began menstruating, and the psychosis cleared up one week after the period. For two weeks she was apparently normal, attending her household duties and going about as usual. At the end of the two weeks the psychosis returned. She again menstruated on the fifth day, and the psychosis terminated one week after the menstrual period. On the third month the psychosis advanced five days and suddenly disappeared with the advent of menstruation. The onset of the psychosis could be noted several days in advance by slight irritability; otherwise the patient was apparently normal during the sane phases.

The cyclic recurrence of the psychosis in the latter half of the menstrual cycle suggested that the condition had some relationship with the hormone balance. This explanation appeared to be most logical, and the institution of endocrine therapy was begun at ovulation. Progesterone[1] 1 mg. was given daily for the first three days. At this time the patient showed signs of increasing nervousness and irritability, fore-

1. The majority of the progesterone used in this case was furnished in the form of progestone by the C. W. Carnrick Company.

casting the probable onset of the psychosis. The dose of progesterone was then increased to 10 mg. daily, with immediate effect on the symptoms. The nervousness and irritability disappeared; the patient became more quiet and calm and continued so with the daily injections. In spite of the dread of the hypodermics, the patient readily admitted that the injections had a most "soothing effect." The cumulative action of the hormone was very apparent. There was practically a minor change of personality. The patient became more congenial and developed an intense interest in both household duties and other diversions. Her mental acumen was far superior to that noted in any of the normal phases since the onset of the psychosis. There was no indication of the recurrence of the psychosis. The 10 mg. doses of the drug were continued until two days before the expected menstrual period. The period was delayed tl..ee days and was normal in all respects. During the injection of progesterone no sedatives or other medications were given.

COMMENT

As this entity was assumed to be of endocrine origin and satisfactory results were obtained with the use of progesterone, the rationale of treatment should be discussed. During pregnancy, progesterone is furnished by the corpus luteum for the first two or three months. At this time the function is taken over by the placenta.[2] The specific action of the hormone is to protect the pregnancy. This is accomplished by suppressing [3] or modifying [4] uterine contractions due to its nullifying effect on the pituitary oxytoxic hormone.[5] There is definite clinical evidence that the hormone has other less important roles. Improvement has been observed in psychosis of pregnancy by the administration of this hormone. Other clinical disorders were effectively relieved by its use. I have noted that the patients who have uterine contractions during the latter months of pregnancy, indicating a deficiency of the hormone, are always of nervous temperament. There is definite indication from clinical observations and from the actual administration that the hormone has some sedative action either directly or indirectly on the central nervous system. During pregnancy large amounts of the hormone are furnished by the placenta. Duyvené de Wit and Oppers [6] found that a placenta weighing 480 Gm. contained 640 micrograms of progesterone, whereas a mature menstrual corpus luteum contained about 16 micrograms.

Since the predisposing cause of postpartum psychosis is the termination of pregnancy, one may well consider the events that take place at that time. The patient is deprived of the baby and the placenta. The loss of the former definitely relieves the patient of an added burden. It should be quite significant that the sudden removal of the placenta, which has been furnishing the patient with a superabundance of progesterone, would not be unlikely to cause a disturbance of the hormone equilibrium. During pregnancy the patient becomes adjusted to the gradual change of ratio between the hormones, the progesterone becoming physiologically increased to serve its purpose. At the termination of pregnancy the patient is suddenly and abruptly deprived of a large store of progesterone, thus disrupting the hormone balance.

Frank [7] in 1931 originally pointed out the imbalance between the estrogenic and corpus luteum hormones. He suggests that "it would thus appear that the continued circulation of an excessive amount of female sex hormone in the blood may in labile persons produce serious symptoms, some cardiovascular, but the most striking, definitely psychic and nervous." Since the corpus luteum hormone is concerned in the metabolism of estrogens, accelerating the excretion of estrogenic hormone,[8] the sudden loss of the placenta would result in an excess of estrogenic hormone in the circulation.

It must be admitted that a psychosis may result from a hormone imbalance, as minor mental changes have frequently been noted in premenstrual tension. Israel [9] suggests that "premenstrual tension is caused by the presence of unantagonized estrogen. This implies that the primary cause is deficient ovarian luteinization with decreased production of progestin." An analogous condition exists following pregnancy, the cause being more apparent than can be explained during the menstrual cycle. This greater disturbance of the hormone balance post partum probably accounts for the more serious mental changes, namely the definite psychosis. A periodic postpartum psychosis may be considered in the same category as an extreme premenstrual tension.

A suitable explanation of why a given patient should develop the psychosis may be found with further study along these lines. It might be interesting to note the significance of the weight of the placenta. The key to the solution may possibly be concerned with the excretory rate of the hormones. Frank [7] also noted in 1931 that "a comparatively small amount of female sex hormone may produce striking effects in a given person if the renal excretory level is high."

Furthermore, the relationship of the corpus luteum to the adrenal cortex may be of some importance. Progesterone has been isolated from the adrenal cortex in considerable quantities.[10] In reporting a series of psychiatric cases, Hoff and Shaby [11] stated that in 4 cases of mental confusion following the puerperium there was good response to the administration of adrenal cortex extract.

The case reported appears to be typical of the condition presenting the usual causes considered by the psychiatrist. Yet the periodic return of the psychosis associated with the menstrual cycle would definitely rule out the commonly supposed causes. The profuse hemorrhage has been noted in a number of the cases reported and occurred in 2 other cases to my personal knowledge. The rather frequent occurrence of the hemorrhage suggests somewhat that the causation is of endocrine origin. The case reports are meager and offer no information of value from the point of view of endocrinology. One report mentioned a cyclic recur-

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10. Wolf, William: Endocrinology in Modern Practice, ed. 2, Philadelphia, W. B. Saunders Company, 1939.

11. Hoff, H., and Shaby, J. A.: Suprarenal Cortical Extract in Acute Confusional States, Lancet **1:** 27 (Jan. 6) 1940.

rence of the psychosis but did not furnish any menstrual data. Kraines,[12] in discussing this condition, states that, "in those patients wherein the menstrual period is associated with emotional disturbances, testosterone propionate has been found useful." The action of this hormone would be the same as that of progesterone as regards their relationship to the estrogenic hormone. Physiologically, progesterone would be the indicated hormone for treatment.

In the 2 other cases familiar to me the psychosis persisted for eight months, during which time menstruation did not occur. It is quite likely that the reestablishment of the menstrual cycle in the case reported was responsible for the psychosis becoming periodic. It may be suggested that in the treatment of the continuous psychosis an attempt be made to reestablish the menstrual cycle by the use of the suitable endocrine therapy, large doses of progesterone being given during that particular phase. The rationale for this is quite apparent.

Time may prove the importance of the corpus luteum hormone in this as well as in other conditions. It no doubt plays the principal role in keeping the patient stable and probably accounts for the feeling of well-being experienced by some during pregnancy as compared to a nervous tension in the nonpregnant state. It is the probable cause for the absence of migraine during pregnancy. The use of the hormone is certainly indicated for the control of minor emotional disturbances frequently noted following delivery. The early use of it may prevent the development of a psychosis. Progesterone may be of definite value in the treatment of certain psychopathic conditions not associated with pregnancy.

In a review of the literature I was unable to find any case report in which the corpus luteum hormone was used as specific therapy for postpartum psychosis. Realizing that 1 case does not constitute definite proof, I submit this report with my impressions so that more complete work may be done by the men who care for these unfortunates, so badly treated by nature.

SUMMARY

The constant precipitating factor and the favorable prognosis for recovery indicate that postpartum psychosis is a clinical entity and is due to some disturbance of a physiologic nature resulting from the sudden termination of pregnancy.

The recurrence of the psychosis associated with the menstrual cycle in the case reported suggested that the condition had some relationship with the hormone balance. The most probable disturbance of the balance would likely be due to the sudden loss of a superabundance of progesterone furnished by the placenta. Excellent results were obtained by the administration of this hormone.

The loss of a large amount of progesterone at delivery and its accepted relationship to premenstrual tension indicate that the psychosis probably results from an excess of this estrogenic hormone in the circulation.

It is suggested that adequate dosage of progesterone be used in the treatment and that the menstrual cycle be reestablished if necessary.

12. Kraines, S. H.: Treatment of Psychiatric States Following Pregnancy, Illinois M. J. **80**: 200 (Sept.) 1941.

Clinical Notes, Suggestions and New Instruments

"CABLE RASH"—A NOTE ON A NEW CLEANSING MIXTURE

GEORGE E. MORRIS, M.D., AND IRVING R. TABERSHAW, M.D., BOSTON

"Cable rash" or "Halowax dermatitis" has been known to the medical profession for more than twenty-five years. Yet in this period of war, as in 1918, cases are being seen of intractable "chloracne" occurring in navy yard workers along both seacoasts, despite the use of the most modern protective creams and ointments. This type of dermatitis is seen also in those engaged in the manufacture of the chlorinated naphthalenes and diphenyls, as well as in men in other occupations

Fig. 1.—Halowax spots before cleansing.

Fig. 2.—1 comparative results of cleansing with mixture described; 2, sulfonated castor oil—note Halowax still present on skin; 3, butyl stearate followed by soap and water, and 4, soap and water—note Halowax still on the skin.

in which these substances are employed. Such cable rashes are thought to be due at least in part to the blocking of the pores by the synthetic waxlike substances whose fumes solidify when they reach the skin. Acute yellow atrophy of the liver has been described as occurring from these chlorinated substances, but the present brief note is not concerned with this phase of their toxicity.

We feel that the removal of all the solid waxlike particles from the skin at the end of each work period would probably prevent the occurrence of this type of dermatitis; with this in mind we have experimented with the removal of these substances from the skin.

From the Division of Occupational Hygiene, Commonwealth of Massachusetts.

A black chlorinated naphthalene (Halowax) was dissolved in chloroform and rubbed into the skin. Various mixtures of soaps, wetting agents and organic solvents were tried, and from the beginning it was obvious that soap and water would not completely remove the wax from the skin. It was finally found that butyl stearate would remove the wax from the pores; this could then be washed off with soap and water, leaving the skin clean. Since this involved two maneuvers, namely, first rubbing the oil well into the skin and then washing with soap and water, it was deemed more practical to evolve a one maneuver cleansing agent.

Such an agent consists of

	Gm. or Cc.
White corn meal	50.0
Butyl stearate	22.5
Sulfonated castor oil (75 per cent oil)	22.5
Oleic acid	5.0

Mix the oils together and then add the corn meal.

This mixture is to be rubbed onto the skin and then removed with water. The procedure should be repeated. Butyl stearate has been found to be a bland, nonirritating substance, and no cases of dermatitis from its use have been reported. At room temperature it is a clear, colorless, odorless, stable oil with a chemical formula $C_{17}COOC_4H_9$. At a temperature below 68 F. it is a solid waxlike substance. It is important to use castor oil which contains 75 per cent of sulfonated oil and 25 per cent of inert material, for oils with greater percentages of inert materials have been found less effective. The accompanying illustrations show the efficacy of this method as compared with the use of soap and water alone or of sulfonated castor oil alone. We suggest that this mixture be tried as a cleansing agent both by workers before the acne develops and by those suffering from the disease.

23 Joy Street.

Council on Pharmacy and Chemistry

PRELIMINARY REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING PRELIMINARY REPORT.

AUSTIN E. SMITH, M.D., Secretary.

STAPHYLOCOCCUS TOXOID (DIGEST-MODIFIED)-LEDERLE

Staphylococcus Toxoid (Digest-Modified)-Lederle was presented by Lederle Laboratories, Pearl River, N. Y., as "staphylococcus toxin treated with pepsin until it will no longer hemolyze rabbit erythrocytes or produce necrosis in the skin of a susceptible rabbit," for the prophylaxis or treatment of infections caused by the staphylococcus. The firm submitted labels, package insert and advertising circular and a galley proof of an article entitled "Staphylococcal Toxoid Prepared by Peptic Digestion" by I. A. Parfentjev, Frances L. Clapp and A. Waldschmidt, which, when presented by the firm, was to appear in the *Journal of Immunology*.

The firm claims that the use of peptic digestion of staphylococcus toxin decreases the possibility of allergic reactions and allows increased dosage of staphylococcus toxoid with less local or general reaction. However, the amount of evidence submitted at the time of presentation does not appear to warrant these claims, and further investigation seems advisable.

In view of this, the Council voted to issue a preliminary statement asserting that at the present time there is insufficient evidence to warrant acceptance of Staphylococcus Toxoid (Digest-Modified)-Lederle for inclusion in New and Nonofficial Remedies, as it appears to be an unessential modification of a toxoid for which the firm is already licensed, but that further consideration will be given to this particular preparation when additional evidence is available.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

AUSTIN E. SMITH, M.D., Secretary.

DEXTROSE (See New and Nonofficial Remedies, 1942, p. 418).

The following products have been accepted:

PACIFIC COAST STERILE SOLUTIONS CO., LOS ANGELES.

Dextrose 5% W/V in Distilled Water: 1,000 cc. bottles. Each hundred cubic centimeters contains 5 Gm. of dextrose.

Dextrose 10% W/V in Distilled Water: 1,000 cc. bottles. Each hundred cubic centimeters contains 10 Gm. of dextrose.

Dextrose 5% W/V in Isotonic Sodium Chloride Solution: 1,000 cc. bottles. Each hundred cubic centimeters contains 5 Gm. of dextrose and 0.9 Gm. of sodium chloride-U. S. P.

Dextrose 10% W/V in Isotonic Sodium Chloride Solution: 1,000 cc. bottles. Each hundred cubic centimeters contains 10 Gm. of dextrose and 0.9 Gm. of sodium chloride-U. S. P.

THEOPHYLLINE WITH ETHYLENEDIAMINE (See New and Nonofficial Remedies, 1942, p. 332).

The following additional dosage forms have been accepted:

H. E. DUBIN LABORATORIES, INC., NEW YORK.

Ampules Solution Aminophyllin: 0.48 Gm. in 20 cc.

Tablets Aminophyllin: 0.2 Gm. (3 grains).

Tablets Aminophyllin: 0.2 Gm. (3 grains) (Enteric Coated).

VITAMIN A (See New and Nonofficial Remedies, 1942, p. 539).

The following product has been accepted:

WHITE LABORATORIES, INC., NEWARK, N. J.

White's Oleo-Blend Vitamin A Capsules: Each capsule contains 25,000 U. S. P. units of vitamin A derived from fish liver oils.

ASCORBIC ACID-U. S. P. (See New and Nonofficial Remedies, 1942, p. 564).

The following dosage forms have been accepted:

WALKER VITAMIN PRODUCTS, INC., MOUNT VERNON, N. Y.

Tablets Ascorbic Acid: 25 mg., 50 mg. and 100 mg.

ISOTONIC SOLUTION OF SODIUM CHLORIDE (See New and Nonofficial Remedies, 1942, p. 425).

The following product has been accepted:

PACIFIC COAST STERILE SOLUTIONS CO., LOS ANGELES.

Isotonic Solution of Sodium Chloride: 1,000 cc. bottles. Each hundred cubic centimeters contains 0.9 Gm. of sodium chloride-U. S. P.

NICOTINIC ACID-U. S. P. (See New and Nonofficial Remedies, 1942, p. 561).

The following dosage forms have been accepted:

WALKER VITAMIN PRODUCTS, INC., MOUNT VERNON, N. Y.

Tablets Nicotinic Acid: 20 mg., 50 mg. and 100 mg.

SODIUM ASCORBATE (See THE JOURNAL, July 10, 1942, p. 883).

The following dosage form has been accepted:

GEORGE A. BREON & CO., INC., KANSAS CITY, MO.

Ampul Solution Sodium Ascorbate: 500 mg. in 10 cc.

SULFANILAMIDE (See New and Nonofficial Remedies, 1942, p. 142).

The following dosage form has been accepted:

HORTON & CONVERSE, LOS ANGELES.

Sulfanilamide Tablets: 0.324 Gm. (5 grains).

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SATURDAY, JANUARY 16, 1943

POLIOMYELITIS INHIBITION

The possibility of aborting experimental poliomyelitis in monkeys by the prophylactic or therapeutic injection of a second neurotropic virus has been suggested by Jungeblut and Sanders [1] of the Department of Bacteriology, Columbia University. Two years ago they adapted the New Haven strain of poliomyelitis virus to white mice by intermediary passage through cotton rats.[2] Thus adapted the virus lost most of its original pathogenicity for monkeys. When it was injected intravenously into monkeys the murine virus was electively localized in the central nervous system, where it persisted for relatively long periods of time without producing symptoms. On recovery from this subclinical infection the monkeys had hardly any acquired immunity against subsequent inoculation with virulent strains of poliomyelitis. This nonpathogenic mutant of virus from monkeys has been propagated for two hundred passage generations in mice, during which time it has increased a thousand fold in pathogenicity for mice with further loss of its immunizing potential for monkeys.[3] The murine virus is readily cultivated in embryonic mouse brain-serum ultrafiltrate.[4] Among their early observations there was suggestive evidence of a strong biologic antagonism between this murine mutant and the virulent parent strain of the virus.

The occurrence of antagonisms between microorganisms is interesting. As far as bacteria are concerned the antagonistic action is usually attributed to specialized enzymes, such as pyocyanase or gramicidin. Virus antagonisms, however, are apparently determined mainly by biologic reactions of tissue cells of the host. Thus the yellow mosaic virus, a mutant of the common light green mosaic disease of tobacco, will not propagate within (or is not propagated by) tobacco tissue cells already infected with the common mosaic disease.[5]

Magrassi,[6] Doerr [7] and others showed that an intracerebral injection of herpes virus following shortly after a corneal or intradermal herpes infection causes a mutual extinction of the effects of both injections. Puntoni [8] noted that a rabbit which receives a series of intravenous injections with fixed rabies virus after a subdural infection with ordinary street virus fails to develop rabies. Hoskins [9] demonstrated that an intramuscular injection of a neurotropic strain of yellow fever virus protects animals against simultaneous infection with a highly pathogenic viscerotropic strain. Findlay and MacCallum [10] found that monkeys inoculated subcutaneously or intraperitoneally with a mixture of neurotropic and pantropic strains of yellow fever usually survive, while control monkeys inoculated with either virus alone usually succumb. Of even greater interest is the antagonism between either canine distemper or lymphocytic choriomeningitis virus and experimental poliomyelitis.[11] Interest here arises largely from the fact that there are no known fractional antigens common to these two interfering agents and the virus of poliomyelitis.

In Jungeblut's studies [2] a similar antagonistic action was noted between his nonpathogenic murine strain and virulent poliomyelitis monkey strains. He found, for example, that an in vitro mixture of murine virus and simian poliomyelitis is often noninfectious on intracerebral injection into monkeys, while the same dose of the simian virus given alone almost invariably caused lethal paralytic symptoms. This antagonism was readily titrated. On testing various virus mixtures, he found that 0.5 cc. of a 1:10 dilution of murine virus would counteract at least a hundred minimum paralytic doses of simian poliomyelitis, irrespective of the simian strain used. Biopsy shows that injection of such a balanced mixture is not followed by propagation of either virus. Symptomless survival from such a balanced inoculation is rarely followed by an appreciable acquired immunity to poliomyelitis.

In a later series of experiments, Jungeblut tested the prophylactic effects of this viable murine vaccine. He found that three to five doses of the murine virus given at daily intervals by the intravenous route from one

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10. Findlay, G. M., and MacCallum, F. O.: J. Path. & Bact. **44:** 405, 1937.
11. Dalldorf, Gilbert; Douglass, Margaret, and Robinson, H. E.: J. Exper. Med. **67:** 333 (Feb.) 1938.

day to two weeks before the intracerebral inoculation with simian poliomyelitis would greatly reduce the paralytic symptoms. Out of 26 monkeys thus treated only 13 developed recognizable paralysis. All of the 19 control monkeys developed partial or complete paralysis. Even more definite antagonistic effects were demonstrated in animals in which the murine vaccine was given therapeutically. Daily intravenous injections of the murine virus were begun three to five days after intracerebral inoculation with the simian virus and continued for five to seven days. Of the 45 monkeys thus treated, 24 (53 per cent) did not show demonstrable symptoms of poliomyelitis. All the 30 untreated controls developed well defined or complete paralysis.

The essential task before the New York investigators at present is the development of a basic theory to explain the observed murine-simian antagonism. The antagonism cannot be explained on the known facts or accepted theories of specific anaphylaxis or immunity. Most theories thus far proposed have been oriented about the known facts of cytologic "blockade" or of cytologic enzyme exhaustion. In his latest study, however, Jungeblut has demonstrated that murine virus partially inactivated by exposure to ultraviolet radiation retains in large measure its prophylactic and therapeutic effects. This strongly suggests that the antagonistic factor is a noninfectious chemical inhibitor formed or secreted by the murine virus. If this can be definitely established, the new "poliomyelitis inhibin" may well prove to be a basic discovery of major practical interest. The work is being continued by the New York investigators.

Meanwhile two additional instances of viral interference of major research interest have been reported by other investigators. Delbrueck and Luria [12] found that a mixed infection of a bacterium with two different strains of bacteriophage, both of them feeding on (or being multiplied by) the same bacterial host, resulted in a complete suppression of the growth of one bacteriophage. Andrews [13] reports that cultivation of influenza A virus in a simple tissue culture renders the culture unable to support the growth of a neurotropic variant of the same strain of influenza A virus. The altered tissue culture, however, is still able to support the multiplication of an unrelated virus, such as lymphogranuloma venereum. Andrews believes the most likely explanation of this "interference" is the using up of enzymes or of specific food materials essential for the growth of the influenza virus. This is essentially a renaissance of the initial Pasteur theory of acquired immunity, which was discarded with the discovery of diphtheria antitoxin.

12. Delbrueck, M., and Luria, S. F.: Arch. Biochem. **1**: 111, 1942.
13. Andrews, C. H.: Brit. J. Exper. Path. **23**: 214, 1942.

DEATHS OF PHYSICIANS IN 1942

During 1942 a total of 3,328 obituaries of physicians were published in THE JOURNAL. Of these, 3,211 were classified as of the United States and 117 as of Canada; 85 were of women. The American Medical Directory Report Service, including the United States, possessions and Canada, recorded 3,580 deaths, including 3,353 for the United States alone, or 142 more than the 3,211 published in THE JOURNAL.

A net increase to the profession of 1,952 resulted from the 5,163 graduates of medical schools in the United States for 1942. The increase does not include graduates of foreign schools who were first licensed in this country in 1942. These statistics are not yet available, but 626 were recorded during the calendar year 1941.

Age.—The average age at death was 65, as compared with 65.9 in 1941 for 3,354 deaths published in THE JOURNAL. Twenty-two physicians died between the ages of 25 and 29, 66 between 30 and 34, 63 between 35 and 39, 83 between 40 and 44, 104 between 45 and 49, 175 between 50 and 54, 278 between 55 and 59, 415 between 60 and 64, 551 between 65 and 69, 548 between 70 and 74, 369 between 75 and 79, 312 between 80 and 84, 178 between 85 and 89, 36 between 90 and 94 and 9 between 95 and 100. The age could not be ascertained on 2 deaths.

Causes.—Heart disease again accounted for the greatest number of deaths among physicians. Coronary thrombosis and occlusion caused 627 deaths, and other coronary diseases and angina pectoris 143. Other diseases of the heart and myocardium were responsible for 838 deaths. In this group cerebral hemorrhage also appears with 393 deaths, arteriosclerosis 250, and cardiovascular renal disease and chronic nephritis 217. Cancer and tumors in various forms accounted for 181 deaths, those of the gastrointestinal tract totaling the largest group of 141. In the general classification, 239 deaths were grouped under diseases of the respiratory system, except tuberculosis. Of these lobar pneumonia was recorded for 23 deaths. There were 139 deaths classified under diseases of the gastrointestinal tract, 40 under diseases of the genitourinary tract, 46 under diseases of the nervous system and 29 under diseases of the blood, including pernicious anemia, leukemia and Hodgkin's disease. Diabetes accounted for 72 deaths, tuberculosis, all forms, for 36, bacteremia, septicemia, pyemia and abscess for 30. Senility and ill defined causes were responsible for 40 deaths, and 38 physicians died following an operation. Rheumatism and arthritis caused 8 deaths, influenza and other infectious diseases 5, disease of the bones and osteomyelitis 4, anaphylaxis and allergy 3, diseases of the thyroid 2 and Addison's disease 2. One death each was recorded from alcoholism, posterior mediastinitis, beriberi, virus pneumonia, tetanus, typhus fever, acute

epidemic hepatitis, psychosis with drug addiction, pellagra, carcinoma following x-ray burns, the result of exposure to x-rays for a number of years, and malaria.

Accidental Deaths.—One hundred and twenty-three accidental deaths were recorded. Automobile accidents accounted for 50 deaths. Falls were responsible for 25 and then airplane accidents 10, trains 7, burns 6, drowning 4, bullet wounds 3, and overdose of medicine, poison and asphyxiation 2 each. A street car accident caused 1 death and illuminating gas 1. The type of accident was not specified for 2 deaths. Fractures, which have been classified under falls, were of the skull, hip and femur. There were 6 unexplained fractures. One death occurred when the physician slipped down an icy mountain slope, and 1 was caused by a ruptured intestine when the physician was squeezed between two operating tables.

Suicides and Homicides.—Forty-seven suicides were recorded, 18 being attributed to bullet wounds. Next in order of classification of method were poison 8, hanging or strangulation 5, cut artery 3, overdose of drugs 2, falls (jumping) 3 and gas 2. One death occurred from injuries received when the physician threw himself under a train. The method was not reported in 5 suicides. Only 1 homicide was reported, a bullet causing death.

Miscellaneous Positions.—Among the decedents were 253 who had been teachers in medical schools, 149 of whom had reached the professorial rank. There were 13 deans. One hundred and twenty had been members of boards of education, 128 health officers, 105 members of boards of health, 59 mayors, 55 coroners, 42 authors, 29 bank presidents, 25 legislators, 18 missionaries, 17 editors, 15 members of city councils, 15 pharmacists, 7 police physicians or surgeons, 6 clergymen, 5 fire surgeons, and 3 each had been judges, lawyers, postmasters and sheriffs. Two were justices of the peace. Three were interns. One was chairman of the revision committee of the Homeopathic Pharmacopeia, 1 was a member of the U. S. Pharmacopeia and 1 had been Secretary of the Interior, Postmaster General of the United States and chairman of the Republican National Committee.

Of the total of 3,211 physicians, 533 had served in World War I, 58 in the Spanish American War and 3 in the Civil War. Thirty-five were members of the U. S. Public Health Service, 20 of the U. S. Army, 15 of the Veterans Administration, 14 of the U. S. Navy and 9 of the Indian Service. One served in the Philippines during the insurrection. Three were members of the National Guard. Six had been members of the medical reserve corps of the U. S. Army and 1 of the reserve of the U. S. Public Health Service; 33 had been medical examiners of draft boards for World War I and 22 for World War II. The classification "Selective Service System" was reported in 17 deaths.

Association Officers.—Among those who died, 2 had been President of the American Medical Association, 3 Vice President, 1 Trustee, 1 member of a Council, 1 secretary of a Council, 1 Vice Speaker, 2 members of the Committee on Medical Preparedness, 17 section officers and 32 members of the House of Delegates. There were 39 presidents of state medical societies, including 1 president of the Alaska Territorial Medical Association. One was president of the Medical Association of the Isthmian Canal Zone. There were 6 secretaries of state societies and 213 presidents of county medical societies.

Military Service.—Eleven physicians died in action during World War II and 37 while in military service. Of those killed in action, 4 died in the Philippine Islands, 1 at Corregidor, 1 when a ship in the Caribbean was torpedoed, 1 somewhere in the Pacific, 1 at Java, 1 at sea (unknown) and 2 at Guadalcanal. Of those who died while in military service, 9 were killed in airplane accidents and 3 were reported suicides. Coronary diseases were responsible for 7 deaths, acute epidemic hepatitis 1, septicemia 1, carcinoma of the sigmoid 1 and uremia 1. Two died when the barracks were destroyed by fire and 1 was killed by the accidental discharge of a sentry's gun, 1 in a shipwreck off the coast of Newfoundland, 2 in automobile accidents and 1 in a train accident. The rest were classified under various physical conditions.

The general total of 3,211 includes deaths that occurred in Turkey, Iran, Scotland, Ecuador, China, Mexico, France, Sweden, Spain, Alaska, Hawaii and Puerto Rico.

Current Comment

SYRUP SUBSTITUTES

Restrictions on the use of sugar have resulted in renewed interest in syrup substitutes. One recent communication[1] presents a brief review of previous discoveries and recommendations in this field. Agents which have been used in the past as sugar substitutes include honey, glycerin, saccharin and molasses. After listing a series of agents used to prepare experimentally artificial syrups containing a water soluble gum and soluble saccharin, the author concluded that syrups of satisfactory stability could be prepared with sodium alginate, irish moss, tragacanth and locust bean gum as thickening agents and saccharin as a sweetening agent. However, because of the uncertainty of the supply of tragacanth and locust bean gum, domestic sodium alginate and irish moss may receive more attention. The thickening agents experimented with by the author include citrus pectin, methyl cellulose, irish moss, acacia, locust bean gum, alginate, apple pectin, karaya gum, glycerin and sorbitol. It is evident that much more work is needed in this field and that the ideal and universal sugar substitute remains to be perfected.

1. Huyck, C. Lee: Syrup Substitutes, J. Am. Pharm. A. **3**, July 1942.

VIRUS (?) PNEUMONIA

An atypical form of pneumonia has recently appeared widely in various areas of the United States. Baker has reported a series of observations which may throw new light on some of the problems engendered by this disease. In a communication to *Science* he[1] reports the isolation of a virus involved in a respiratory tract infection in cats, observed in the past year in the northeastern part of the United States. The main characteristics of the disease in cats are its highly infectious nature, debilitating effects and long course. Its respiratory nature is recognized by sneezing and coughing, which is accompanied by a mucopurulent discharge from the eyes and the nose. The existence of pneumonia is not ordinarily determined by the usual clinical examination, but necropsy reveals grayish densely consolidated areas in the anterior lobe of the lungs. The virus was obtained by inoculating intranasally into mice suspensions of lungs from cats with typical clinical symptoms. The agent was easily transferred to eggs, which had been incubated for five days, by inoculation into the yolk sac. Attempts to pass the agent through Berkefeld filters gave irregular results. The nature of the agent, however, became apparent when sections of the yolk sac membrane stained by a suitable means revealed numerous elementary bodies similar to those of psittacosis. Centrifugation of the infected mouse lungs and yolk sac suspensions removed much of the infective agent from the supernatants and concentrated it in the sediments. This is added evidence that the observed elementary bodies are the etiologic agents. A number of instances of contact between sick cats and people who subsequently developed atypical pneumonia have appeared. Complement fixation tests have been made, but the results in both cats and man have so far been somewhat inconclusive. The conclusion is, however, that this respiratory disease in cats is due to a virus that forms elementary bodies and that this virus is the same as or crossrelated to the one causing at least some of the cases of so-called atypical or virus pneumonia in man. In another preliminary communication from Eaton and his colleagues[2] an infectious agent from cases of virus pneumonia was transmitted to cotton rats. Of 131 cotton rats receiving material from cases of virus pneumonia, 35 developed lung lesions. By serial intranasal passage of lung suspensions from animals which developed lesions on the first passage, strains of an infectious agent from 6 cases of virus pneumonia were adapted to cotton rats. After four to six passages the adapted strain produced gross evidence of lung involvement in over 90 per cent of the animals inoculated but seldom caused death. The lung lesions were patchy red-gray in appearance. Microscopic examination of sections of lungs showed an infiltration of the septums with polymorphonuclear leukocytes and mononuclear cells and hyperplasia of the alveolar epithelium. By cross inoculation and neutralization tests, antigenic relationships between six established strains were demonstrated. Cotton rats immunized by two successive intranasal inoculations with adapted strains were solidly immune to reinoculation with a specimen of infectious human lung which produced definite lesions in control animals. The appearance of nonbacterial lung lesions in cotton rats after inoculation of material from cases of virus pneumonia suggests that a virus-like agent was transmitted and established by serial passage. Strains adapted to cotton rats were related to the agent in human material by cross immunity tests. This agent, which is presumably a filtrable virus, differs from the psittacosis-like virus and from other known viruses which can infect cotton rats by the intranasal route. Eaton and his co-workers conclude that at present the evidence for the causal relation of this agent to the most common form of "atypical pneumonia" must be considered incomplete because of irregularities in the neutralization tests, particularly those with human serum.

1. Baker, James A.: A Virus Obtained from a Pneumonia of Cats and Its Possible Relation to the Cause of Atypical Pneumonia in Man, Science **96**: 475 (Nov. 20) 1942.

2. Eaton, M. D.; Meikeljohn, Gordon; Van Herick, William, and Talbot, J. C.: An Infectious Agent from Cases of Atypical Pneumonia Apparently Transmissible to Cotton Rats, Science **96**: 518 (Dec. 4) 1942.

MEDICOLEGAL CASES: 1936-1940

The House of Delegates in 1932 adopted a resolution suggesting the publication in book form of the medicolegal abstracts that are weekly printed in THE JOURNAL. An initial volume was published that year containing the abstracts that had previously appeared in THE JOURNAL during the calendar years 1926-1930. In 1936 a second volume, also covering a five year period, was published. Now a third volume is available which includes abstracts published from 1936 to 1940 inclusive. These books are bound in durable library buckram, are adequately indexed to enable the user readily to find a discussion by the courts of the particular medicolegal problem that prompts his search and contain complete tables of cases giving complete titles to all the cases abstracted. The current volume includes over eight hundred abstracts. The cases abstracted deal with a wide variety of subjects of interest to physicians and others concerned with matters of medicolegal import. A seventy-four page index begins with reference to cases involving abandonment of patients in relation to malpractice and concludes with a refereñce to a court discussion on zoning regulations as they apply to mental and nervous disease hospitals. Between these two index subjects are to be found references to practically all the important reported decisions of courts during the five year period in which joint issues of medicine and law have been involved. As reference sources these volumes are unique in their field and they should be in every library, legal as well as medical. The preface to the second volume called attention to an oft repeated truism that a man who acts as his own attorney has a fool for a client and to the fact that the idea prompting the publication of these abstracts in THE JOURNAL and in book form has not been to qualify physicians to assume the role of counsel for themselves or for others. Rather the idea has been to exemplify the medicolegal problems that have been before the courts so that physicians may more intelligently meet such problems when they arise in their own personal experiences and perhaps to aid physicians in avoiding some of the pitfalls into which their fellow physicians have fallen.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war and such other information and announcements as will be useful to the medical profession.

DIABETES AND MILITARY SERVICE

ELLIOTT P. JOSLIN, M.D.
Boston

Liberally estimated there are about 800,000 living persons with diabetes in the United States, and one might suppose that among them would be many who could serve their country as members of the armed forces. However, when one looks at the problem more closely and studies it from a statistical point of view, the number of those who could serve usefully dwindles to so few that it would not make their selection worth while. Furthermore, after induction, the impossibility of always assuring a proper diet, the possibility of increase in severity even among those not taking insulin when inducted, the recurring necessity for creation of medical boards to decide on their physical status when transferred from station to station or when hospitalized for any trivial ailment, combined with the responsibility of the government for their care during the rest of their lives, uphold the present rule to forego their services. Especially does this seem wise when considered in connection with the need for workers in civilian life.

Diet and Insulin at Least Ten Years After Their First Visit of 139 Diabetics Selected as Possible Candidates for the Armed Forces

Use of Insulin	Unrestricted Diets	Restricted Diets	Total
No insulin	94	11	105
Insulin irregularly	1	3	4
Insulin regularly (5 unknown)	3	22	25
Total	98	36	134

Statistically one can assume that two thirds of the 800,000 persons in the country who have diabetes are above the age of 40 years and of the remaining one third only two fifths are males. From the 107,000 males with diabetes under 40 years of age one must again deduct about 17,000 under 18 years of age, thus leaving by such an estimate around 90,000 total diabetic males between the ages of 18 and 40 years. In all probability not more than 10 per cent and far more likely 5 per cent would meet army requirements, and when one allows for disbarment because of dependents and other nonphysical reasons the final number available for induction would surely not exceed 4,500 and more likely 2,250 individuals.

If one bases statistical reasoning on the number of diabetic persons, assumed as 800,000 for the whole country and allocated according to the age distribution of the National Health Survey as applied to the population of 1940, the total for ages 18 to 44 is only a little over 50,000 and between 18 and 39 years about 36,000. These allocations were made for me by the Statistical Department, Metropolitan Life Insurance Company. Assuming 5 per cent available there would be only 2,500 to 1,800 men.

A third method is open for appraising the number of those who are diabetic who could be considered army material. This is to make a study of a series of diabetic persons. For this purpose the first 10,000 cases coming for diabetes to our clinic were examined. Of this number approximately 15 per cent had benign glycosuria and not true diabetes as diagnosed when first seen; only those cases diagnosed as diabetic were included in this study. Among this group of 8,500 there were 780 males between the ages of 18 and 39. Of this 780 there were only 139 who could be considered eligible for the draft; 641 would have been ineligible because of either physical defects or severity of diabetes.

The average age of the 139 available at their first visit was 31.1 years. Already they had had diabetes 2.2 years when first seen. By 1942, ten years after the last of the 139 had come to the office, the surviving patients of the original 139 numbered 126, 13 having died (9.4 per cent). The causes of death were coronary disease 7, pneumonia 3, tuberculosis 1, coma with infection 1, and 1 death with the diagnosis of diabetes with hypertension and nephrosis.

Insulin was not taken when the patients were first seen, with the exception of 1, who had a dose of 5 units of insulin on one day during a five day stay at the hospital. Data for subsequent use of insulin and data regarding dietary habits are shown in the accompanying table. According to the table, which included both living and those who had died, 105 patients are still taking no insulin as reported by various follow-up letters, later check-ups or return visits. Four were taking insulin irregularly and 25 regularly, varying over a period from one to ten years from the time of first observation, thus evidently having contracted diabetes at least of moderate severity.

Ninety-four of the original 139 patients were on unrestricted diets, eating everything, but "light on pastries and sweets." Eleven were on moderately restricted diets.

As reported in the 1942 follow-up letters, 102 patients were well and considered themselves in good health. Most of them were working at the time, although many had had a complication of some sort since their first visit. These complications, arising from the time since they were first seen, as reported by the patients or their doctors, included carbuncles 2, abscesses and infections of the skin 7, duodenal ulcer 5, disease of the gallbladder 4, arteriosclerotic impairments including cardiac changes 9, arthritis 3, bursitis 2, thyroid disease 2, colitis 2, fractures 1, varicose veins 1, sinus infection 1, genitourinary 1. These complications were

the only ones reported or that came under observation. There would be, obviously, many more not reported in a period from forty years ago, when the first patient was seen.

Among those later taking insulin, 4 were subject to reactions, including 1 with severe reactions. One patient had coma twice, and another's diabetes became very difficult to control.

If the 139 cases culled from the entire 10,000 glycosuric or 8,500 diabetic are utilized for computing the total number of the 800,000 in the country diabetically available, we have 13,062 individuals. Since these are 31.1 years old when first observed by us, the number with dependents and in essential occupations would be unusually large quite apart from physical considerations, and it should be safe to reduce these figures by two thirds to approximately 4,000 men.

It thus appears both by arbitrary statistical estimates as well as by computations, based on an actual study and selection from a series of 8,500 persons diagnosed as having diabetes, that in the United States today the number of diabetic persons available for the Army or Navy lies between 4,500 and 1,800 men. With these figures in mind, the diabetic quota useful for military service is relatively so insignificant, the hazards which both the diabetic and the government would undergo if they were inducted are so great and the need for their services in civilian occupations, where they would be less exposed to complications, so apparent, that the present rule to omit them from the draft appears proper.

ARMY

NEW BRIGADIER GENERALS

Col. Albert W. Kenner of the U. S. Army Medical Corps has been promoted to brigadier general for his highly efficient work in North Africa. This is the officer to whom Brig. Gen. Larry McAfee, the assistant surgeon general, referred in his opening remarks in the first broadcast, December 26, sponsored by the American Medical Association in the present radio program entitled "Doctors at War." Among other things, General McAfee said "I cite with keen pleasure the fact that one of the senior surgeons of the North African task force was promoted to brigadier general in recognition of his highly efficient operation of the medical field service in the face of greatest difficulties." General Kenner was born in Massachusetts in 1889, was awarded a Ph.D. in 1910 and an M.D. in 1915 at George Washington University, and graduated from the Army Medical School in 1917, in which year he was commissioned in the medical corps. He has been awarded the Distinguished Service Cross, the Silver Star and the Purple Heart.

Col. Fred W. Rankin, M.C., President of the American Medical Association, senior consultant in surgery, and Col. Hugh Jackson Morgan, M.C., senior consultant in internal medicine in the office of the Surgeon General, Washington, D. C., have been created temporary brigadier generals.

AUTHORIZE CORPS OF PHYSICAL THERAPY AIDES AND OF DIETITIANS

The President has signed the bill (H. R. 7633) which authorizes the creation of a corps of physical therapy aides and a corps of dietitians in the Army of the United States. According to the *Army and Navy Journal* the members of these corps will come largely from physical therapists and dietitians now on duty with the medical department on a civil service status. The desire to send these women overseas and to protect their rights as belligerents is responsible, it is said, for the plan to give them military status. In general, military pay, including allowances, will be the same or slightly more than civil service pay. The act authorizes a director of each of these corps with relative rank of major, with other members holding relative rank of captain, first lieutenant and second lieutenant. Pay of members of the corps would be the same as pay of regular army officers without dependents of the fourth, third, second and first pay periods.

PAY OF ARMY AND NAVY NURSES INCREASED

The President has signed a bill (H. R. 7633) which increases the pay of army and navy nurses. As far as the act relates to nurses, it accomplishes two objectives: (1) it gives nurses pay of their relative rank and (2) it provides increased relative rank for some nurses. In explanation the *Army and Navy Journal* says that nurses and head nurses have relative rank of second lieutenant and will receive the pay of the first pay period ($1,800), together with allowances. Chief nurses have relative rank of first lieutenant and will receive the pay of the second pay period ($2,000) together with allowances. The new bill gives relative rank of colonel and pay for the sixth pay period ($4,000) to the superintendent of the army nurse corps. All ranks, in addition to base pay, will receive longevity at 5 per cent for each three years of service up to thirty years. A clause in the act protects some nurses who would have lost pay under the new act.

LARGE CLASS OF MEDICAL ADMINISTRATIVE OFFICERS

A large class graduated on December 19 from the Medical Administrative Officer Candidate School operated at Camp Barkeley, Texas, by the Medical Replacement Training Center. This class was four times the size of the class graduated in September. The ceremonies were attended by distinguished guests, including Major Gen. Henry Terrell Jr., commanding general of the 90th Motorized Division stationed there; Col. Henry A. Finch, Camp Barkeley commander; Hon. Will W. Hair, mayor of Abilene; Malcolm Meek, president of the Citizens National Bank of Abilene; Dean Walter H. Adams of Abilene Christian College, Dean W. B. McDaniel of McMurry College and Dr. William T. Walton, vice president of Hardin-Simmons University.

The address by the Surgeon General of the Army, Major Gen. James C. Magee, was read by Col. Frank Wakeman, and the diplomas and commissions were presented by Brig. Gen. Roy C. Heflebower, commandant of the Medical Replacement Training Center. In this largest officer candidate school class were thirteen Negroes receiving commissions as second lieutenants, the largest colored contingent to date. After the ceremonies the new officers were given ten day graduation leaves prior to reporting to their first stations for assignment to duty.

THREE HOTELS AT MIAMI BEACH TAKEN OVER BY ARMY

Three of the largest hotels at Miami Beach, the Pancoast, the Tower and the Gulf Stream apartments, were taken over by the War Department on December 17 for conversion into hospitals for the Army Air Forces. The hotels were obtained by leases. Of the three the Pancoast is the oldest, built in 1923; the Tower was built in 1935 and the Gulf Stream apartments in 1925.

ARMY PERSONAL

Dr. William C. Menninger, Topeka, Kansas, has been commissioned lieutenant colonel in the U. S. Army Medical Corps and assigned to duty as consultant in psychiatry.

NAVY

THE NAVY NEEDS YOUR BINOCULARS

The U. S. Navy sometime ago made an urgent appeal to all persons in the United States who own binoculars to offer them to the Navy, and only six thousand persons in the entire country have done so.

In the first world war more than fifty thousand binoculars were offered, and of those which were accepted all but one were returned to their owners at the end of the war. Optical firms in this country are doing their best to meet the demands of our military forces, but the making of binoculars requires special materials, time and skill. The problem is further complicated by the great demands of the air forces, which require special optical instruments, such as the stereoscopic height finder and the "elbow telescope."

NAVY PERSONALS

The name of Capt. Edward C. White, U. S. Navy Medical Corps, was sent to the Senate with recommendation for promotion to rear admiral. Captain White was head of the Inspection Division of the Bureau of Medicine and Surgery in Washington.

Lieut. (j. g.) Beulah Ann Buchanan, U. S. Navy Nurses Corps, chief nurse of the U. S. Naval Hospital at Great Lakes, Ill., is being relieved from duty there to report for service outside the continental United States. Her position will be taken over by Lieut. Mary Martha Heck, U. S. N. N. C., who has been transferred from Quantico, Va.

Dr. George M. Caldwell, formerly resident physician at the Greenbrier Hotel, White Sulphur Springs, W. Va., has been commissioned a lieutenant in the U. S. Navy and is stationed at Norfolk, Va.

CIVILIAN DEFENSE

NURSING EXECUTIVES FOR EMERGENCY BASE HOSPITALS

The Office of Civilian Defense, Washington, D. C., has issued Circular Medical Series No. 24, which states that the Surgeon General of the United States Public Health Service has authorized the appointment of a limited number of qualified nurses with supervisory and administrative experience who could be sent to emergency base hospitals, when activated, to serve as nursing executives. They will be offered appointments in the Public Health Service on an inactive status and will be called to active duty by the Surgeon General on the recommendation of the state chiefs of Emergency Medical Service and regional medical officers only if their services are required at emergency base hospitals because of a military necessity. When on duty they will be entitled to payment by the Public Health Service according to their experience and qualifications at per diem rates based on annual salaries of $2,600 or $2,300 and necessary travel and maintenance when away from their usual places of residence.

The number of such nurses to be recruited in each state should be equivalent to twice the number of affiliated units actually being formed in that state. Qualified nurses should be nominated by coastal state chiefs of Emergency Medical Service in consultation with the state nurse deputy and the directors of affiliated units in his state.

For appointment in the United States Public Health Service, candidates must have not less than two years' experience in hospital ward or operating room supervision in a hospital approved by the American College of Surgeons and the American Medical Association. They must be under 55 years of age and in good physical condition. Although their appointments obligate them to serve in an emergency base hospital in their regions if called to duty by the Surgeon General in a wartime emergency, they may resign their appointments in the Public Health Service at any time to accept assignments in the Army or Navy.

State chiefs of Emergency Medical Service may obtain the necessary application forms for these appointments from the regional medical officers. These forms should be filled out and sent to the appropriate state chief of Emergency Medical Service who will transmit them, with his approval, to the regional medical officer, who will forward the applications with his endorsement to the Emergency Medical Section, United States Public Health Service, 2000 Massachusetts Avenue, Washington, D. C.

MISCELLANEOUS

AMERICAN OPTICAL COMPANY AWARDED ARMY-NAVY E

Ceremonies were conducted at the headquarters of the American Optical Company, Southbridge, Mass., Nov. 30, 1942, for the award of the Army-Navy E. This award comes from combined Army and Navy boards of recognition for the quantity and quality of output, the avoidance of work stoppages, the overcoming of production obstacles, the training of additional labor forces, capable management, utilization of subcontracting facilities and satisfactory records on health, accidents, working conditions and plant protection. The award consists of a flag to be flown above the establishment and of a lapel pin to be worn by each employee of the company, symbolic of their contribution to victory in this war. The award was presented to the American Optical Company by Brig. Gen. Burton O. Lewis and was accepted by George B. Wells, president of the company. This company has been producing optical goods for one hundred and nine years and many of its products today are aiding in the war effort. The company, in cooperation with the Surgeon General's Office, has designed a mobile optical unit to handle spectacle repairs in the field, and several of these units have already been built. The company supplies goggles for aviators, ski troops, navy lookouts and gunners and for mechanized troops, as well as for industrial workers on the home front. The company has made a wide variety of diagnostic and examining instruments for examining recruits and aiding in guarding the vision of service men.

BOOKS FOR RUSSIAN MEDICAL STUDENTS

Students in the First Kharkov Medical Institute formerly at Kharkov, Russia, have written letters of appreciation to the Russian War Relief, Inc., for American medical textbooks, which have been sent by the hundreds to the Soviet Union to help prepare more doctors for work with the Russian army. When the Germans occupied Kharkov, the Kharkov Institute, one of the largest medical schools in the world, was moved to Chkalov, where classes were in full swing within a week after the student body and faculty left Kharkov. Russian War Relief, Inc., is seeking to send still more of all kinds of up to date medical textbooks for Soviet medical students. Contributions for this purpose may be sent to Russian War Relief, Inc., 11 East 35th Street, New York City.

INFECTIOUS DISEASES IN GERMANY

The *Reichsgesundheitsblatt* (Berlin) of July 29 contains the figures for the infectious diseases in Germany during the first half of 1942:

	1942	1941
Diphtheria	121,602	82,238
Scarlet fever	220,076	125,524
Tuberculosis (lung and throat)	68,500	63,998
Tuberculosis (other organs)	9,693	8,390
Infantile paralysis	609	420
Typhus	2,918	2,552

There were 1,205 cases of bacterial food poisoning as against 947 cases in the first half of 1941.

ORGANIZATION SECTION

MEDICAL LEGISLATION

DISTRICT OF COLUMBIA

Bill Introduced.—H. R. 33, introduced by Representative Burdick of North Dakota, proposes to prohibit experiments on living dogs in the District of Columbia.

MEDICAL BILLS IN CONGRESS

Bills Introduced.—H. R. 98, introduced by Representative Smith, Maine, a bill to create a Division of Water Pollution Control in the United States Public Health Service. H. R. 317, introduced by Representative Fitzpatrick, New York, proposes to amend the Social Security Act so as to provide for the payment of benefits to permanently and totally disabled individuals. H. R. 348, introduced by Delegate Dimond, Alaska, proposes to extend the benefits of the United States Public Health Service to fishermen. H. R. 361, introduced by Representative Magnuson, Washington, proposes to authorize the construction of a Veterans' Administration general medical and surgical hospital and domiciliary facility in western Washington. H. R. 369, introduced by Representative Myers, Pennsylvania, proposes to prevent discrimination against blind persons and persons with impaired visual acuity in the administration of the civil service laws and rules. H. R. 370, introduced by Representative Myers, Pennsylvania, proposes to extend the federal old age benefit provisions of the Social Security Act to certain nurses in respect of their employment outside of religious, charitable and other nonprofit institutions. H. R. 492, introduced by Representative Angell, Oregon, proposes to extend the benefits of the Social Security Act to include individuals who are physically disabled. H. R. 493, introduced by Representative Angell, Oregon, proposes to authorize the Secretary of the Interior to locate, establish, construct, equip and operate a hospital for the insane of Alaska. H. R. 496, introduced by Representative Angell, Oregon, proposes to provide for the education of all types of physically handicapped children. H. R. 649, introduced by Representative Bulwinkle, North Carolina, proposes to provide for the reorganization of the United States Public Health Service. H. R. 655, introduced by Representative Ludlow, Indiana, proposes to provide for suitable recognition of the voluntary services of civilian nurses with the Army during the influenza epidemic. H. R. 658, introduced by Representative Rogers, Massachusetts, proposes to provide prosthetic appliances to certain veterans suffering from non-service connected disabilities. H. R. 665, introduced by Representative Rogers, Massachusetts, proposes to provide medical and hospital treatment and domiciliary care for members of the Women's Army Auxiliary Corps on a parity with members of the Women's Reserve of the Navy. H. R. 667, introduced by Representative Rogers, Massachusetts, proposes to authorize an appropriation to provide additional hospital and outpatient dispensary facilities for persons entitled to hospitalization in Veterans' Administration facilities. H. R. 669, introduced by Representative Rolph, California, proposes to provide compensation for personnel sustaining disease or injury while performing civilian defense duties. H. R. 691, introduced by Representative Dickstein, New York, proposes to establish federal medical academies. H. R. 699, introduced by Representative Barden, North Carolina, proposes to provide vocational rehabilitation, education, training and other services to persons disabled while members of the armed forces or disabled in war industries or through other causes or those congenitally disabled, and to render such persons fit for service in war industry, agriculture or other useful civilian industry.

STATE MEDICAL LEGISLATION

Massachusetts

Bills Introduced.—H. 44 proposes to authorize transfer to a hospital of prisoners being held for sentence or trial, where it appears from a physician's certificate that such prisoner requires medical treatment which cannot safely or properly be given in the prison. H. 79 proposes to amend the medical practice act by adding a new paragraph authorizing the periodic inspection of colleges, universities and medical schools approved for the purpose of medical education. When the approving authority determines that such school does not meet the requirements necessary for approval it shall send written notification thereof to the proper school authority specifying what steps the school must take in order to prevent the withdrawal of approval. Provisions are then made for a hearing on behalf of the medical school in the event it objects to the finding of the approving authority. H. 80 proposes to amend the medical practice act by providing that an applicant who has failed to pass a second examination given by the board will not be entitled to be examined on a new application until after the expiration of one year following the second examination nor unless he shall furnish the board with satisfactory proof that he has completed a postgraduate course of one year in a legally chartered medical school approved by the board. H. 81 proposes to amend the medical practice act by changing the list of subjects which an applicant for license to practice must have studied. The new list proposed includes the subjects of anatomy, physiology, pathology, biochemistry, bacteriology, immunology, public health, pharmacology, materia medica, pediatrics, medicine, surgery, obstetrics and gynecology. This proposal would omit the subjects of chemistry, biology, physics, psychiatry and hygiene required under the prior law. H. 84 proposes to amend the premarital examination law by authorizing the requisite certificate to be signed by a physician registered or licensed to practice in any state or a commissioned medical officer on active service in the armed forces of the United States or in the United States Public Health Service. Previously only physicians registered in Massachusetts were authorized to sign the required certificate. The proposal then provides that the examination shall consist of a general medical examination and shall include a standard serologic test for syphilis and such other laboratory tests as are indicated by the general medical examination, and the serologic test for syphilis shall be made in a laboratory meeting standards approved by said department and sets forth the form of the certificate which the examining physician must execute.

New Jersey

Bills Enacted.—A. 412 has become chapter 342 of the Laws of 1942. It amends section 45:9-8 of the medical practice act by requiring an applicant for licensure to prove that his medical education extended over a period of not less than four full school years, including "four satisfactory courses of lectures of at least eight months each" either "consecutively or in four different calendar years." The "consecutively" is new and is for the purpose of permitting graduates of such accelerated medical courses to obtain licensure in New Jersey, but the school of graduation must still, of course, be "in good standing in the opinion of the board." S. 358 has become chapter 346 of the laws of 1942. It amends certain sections of the present law regulating the practice of nursing in the following particulars: (1) Present registration requirements may be waived where the applicant meets the requirements that were in existence at the time of his or her graduation from an approved school of nursing, or the requirements existing on April 1, 1914 if the graduation was prior to that date; (2) reciprocal registration of qualified Canadian licentiates is authorized; (3) the age limit of students who may be admitted to an approved school of nursing is lowered from 18 to 17½ years during the period of the war and for six months thereafter; (4) the fee for the issuance of a certificate of registration is no longer necessary. A fee of one dollar will still be charged, however, each time the certificate is annually renewed.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Changes in Health Officers.—Dr. Caroline H. Callison, Chatom, will serve as health officer of Washington and Clarke counties. —— Dr. Elisha Moore, Livingston, health officer of Sumter County, has also been placed in charge of the Greene County department of health.——Dr. Julius E. Dunn, Florence, is the new health officer of Etowah and Calhoun counties, with headquarters in Anniston.

DELAWARE

State Medical Election.—Dr. Lawrence J. Jones, Wilmington, was elected president of the Medical Society of Delaware at its recent annual meeting, to serve for one year beginning January 1, and Dr. William O. LaMotte, Wilmington, was named secretary. The next annual meeting is planned for Wilmington on October 12 and 13.

ILLINOIS

Special Advisory Committee on Industrial Hygiene.—Governor Green has appointed the first special advisory committee to the division of industrial hygiene of the Illinois Department of Public Health. Members of the committee are Drs. Roland R. Cross, Springfield, state director of public health, and Milton H. Kronenberg, Chicago, chief of the division of industrial hygiene, ex-officio members; Philip H. Kreuscher and Joseph H. Chivers, Chicago, chairman and vice chairman, respectively; Dr. Raymond B. Allen, executive dean, Chicago Colleges of the University of Illinois; William H. Donovan, Harry Guilbert, A. G. Hewitt and Oliver E. Mount, Chicago; Dr. Nordahl O. Gunderson, Rockford; Charles G. Lanphier, Springfield; Edward F. Schweich, East St. Louis, and Dr. Harold A. Vonachen, Peoria. The new committee will aid in the development of state programs of adult hygiene, including the control of hazardous working conditions and the care of pregnant women in war industries.

Chicago

Personal. — Evelyn B. Tilden, Ph.D., of the Rockefeller Institute for Medical Research, New York, has been appointed associate professor of bacteriology at Northwestern University Medical School.——Dr. William H. Lipman, medical director of Swift & Company, retired, January 2, having reached his sixty-fifth birthday. Dr. Lipman graduated at the University of Illinois College of Medicine in 1904 and joined Swift & Company in the same year.

Joint Meeting on Cancer.—A joint meeting of the North Side Branch of the Chicago Medical Society and the Institute of Medicine of Chicago will be addressed on January 20 at the Chicago Woman's Club by Drs. Paul E. Steiner on "Significance of Recent Research on the Causation and Nature of Cancer and the Role of the Clinician in Further Advance; Charles B. Huggins, "Function of the Prostate and Its Relation to Tumors," and Vernon C. David, "Carcinoma of the Large Bowel."

Alien Physicians Eligible for City Positions.—Corporation Counsel Barnet Hodes, in an opinion, December 17, said that alien interns and resident physicians may be hired on a temporary basis for work in the Municipal Contagious Disease Hospital, newspapers reported. Dr. Herman N. Bundesen, president of the board of health, requested Hodes' opinion after he said his advisory board reported that it would be necessary to close the hospital January 1 if a supply of alien physicians could not be obtained, it was stated.

INDIANA

Personal. — Dr. Robert W. Reid, Union City, has been appointed health officer of Randolph County to succeed Dr. Andrew M. Brenner, Winchester, who has entered the Navy. ——Dr. Joseph L. Allen, Greenfield, has been named coroner of Hancock County.

Society Publishes Service Bulletin. — The St. Joseph County Medical Society, South Bend, brought out its new Service Bulletin in November. The first issue contains twelve mimeographed pages designed primarily to let the men in service know what is going on at home.

Society News.—Dr. Byrl R. Kirklin, Rochester, Minn., addressed the Indianapolis Medical Society, November 24, on "Bleeding Lesions of the Gastrointestinal Tract," and the Indiana Roentgen Society on "The Military Situation as It Pertains to Radiologists." —— The Spencer County Medical Society, at a meeting in Rockport, December 15, decided to forego all regular meetings for the duration of the war because of the small number of members remaining. Meetings will be called to transact special business only.——Dr. Maximilian Kern, Chicago, discussed "Endocrinological Types of Obesity" before the La Porte County Medical Society in La Porte, December 17.

KANSAS

Society News.—The Sedgwick County Medical Society was addressed in Wichita, November 3, by Drs. Hugh G. Jeter and Harry Wilkins, both of Oklahoma City, on "Paracentetic Fluid as an Aid in Diagnosis" and "Injuries to the Covering of the Brain" respectively.

Coroners Appointed.—Governor Payne H. Ratner recently made the following appointments to the position of coroner: Drs. Wardie W. Weltmer, Beloit, of Mitchell County to succeed Dr. Richmond E. Bennett, and Dr. Claud F. Young, Fort Scott, of Bourbon County to succeed Dr. Laurence L. Cooper. Dr. Bennett and Dr. Cooper are in military service.

KENTUCKY

Jane Todd Crawford Day.—On Dec. 13, 1942 the first Jane Todd Crawford Day was observed. The day was set apart by an official proclamation of the governor as a part of the sesquicentennial year program commemorating Kentucky's one hundred and fiftieth year of statehood. To mark the event, the woman's auxiliary section of the state medical journal was recently dedicated to a review of the first ovariotomy performed by Dr. Ephraim McDowell. The cover of the special edition carries a picture, "Dawn of Abdominal Surgery," executed by Dean Cornwell for John Wyeth and Brother, Inc., Philadelphia. The inside cover contains a reproduction of "Beaumont and St. Martin," another of the series sponsored by Wyeth and Brother. An article on Jane Todd Crawford by George Madden Martin, Louisville, narrates the complete story of the first ovariotomy performed by Dr. McDowell in a pioneer cabin in Danville on Dec. 25, 1809.

MASSACHUSETTS

Public Lectures. — A course of free public lectures on medical subjects opened in the Peter Bent Brigham Hospital Auditorium, Boston, January 3, under the auspices of the Harvard Medical School. Dr. George W. Thorn, Boston, gave the first lecture on "The Role of the Endocrine Glands in Adaptation," and Dr. Joseph W. Ferrebee, Boston, the second, January 10, on "Newer Knowledge of Vitamins." Other speakers in the series are:

Dr. Frank H. Lahey, Boston, January 17, The Supply of Doctors.
Dr. Fredrick J. Stare, St. Louis, January 24, How Best to Eat Under War Conditions.
Dr. Maxwell Finland, Boston, January 31, Common Colds and Their Complications.
Lieut. Col. Alexander Marble, M.C., U. S. Army, February 7, The Care of Soldiers in an Army Hospital.
Constantin P. Yaglou, M.M.E., Boston, February 14, Problems of Ventilation in the Home.
Dr. Arlie V. Bock, Cambridge, February 21, Civilian Physical Fitness as a War Measure.
Dr. Allan M. Butler, Boston, February 28, Healthy Children.
René J. Dubos, Ph.D., New York, March 7, Antiseptic and Chemotherapeutic Agents.

Library Fund Named for Dr. Wilinsky.—On Dec. 20, 1942 special ceremonies were held at the Beth Israel Hospital, Boston, to celebrate the sixtieth birthday of Dr. Charles F. Wilinsky, executive director and superintendent of the hospital and formerly deputy commissioner of health of Boston. Dr. Wilinsky was presented by Judge Abraham E. Pinanski, Boston, with a bound volume of congratulatory letters from all parts of the country. Judge A. K. Cohen turned over a sum of money to be known as the Charles F. Wilinsky Library Fund, and Mrs. Pinanski spoke for the hospital auxiliary in presenting a fund for the hospital in his name. A portrait of Dr. Wilinsky, painted by Jacob Binder, was unveiled by Dr. Samuel A. Robins, Boston. Mr. James A. Hamilton, New Haven, Conn., president of the American Hospital Association, also spoke. The *New England Journal of Medicine* commented editorially on Dr. Wilinsky's birthday in special tribute. Dr. Wilinsky graduated at the Baltimore University School of Medicine in 1904. He was associated for many years with the Boston Health Department. In 1927, as deputy commissioner of health, he was granted a leave of absence to assist in a survey on the health of Palestine. For many years he

was in charge of the health units that were established in the city through the George Robert White Fund. In 1935 Dr. Wilinsky was also in charge of a relief project for resident physicians of Boston. He became superintendent of the new Beth Israel Hospital in 1928. He is president of the Massachusetts Hospital Association.

MICHIGAN

Special Lectures.—Dr. Edward R. A. Merewether, London, England, gave a special informal lecture before the Wayne County Medical Society in Detroit, December 21, on "The Latest Medical Facts from Abroad." A joint meeting of the society and the Detroit Pediatric Society was addressed, December 14, by Dr. John Harry Ebbs, associate in pediatrics, University of Toronto Faculty of Medicine, Canada, on "Nutrition in Everyday Practice."

Report on Child Guidance Program.—Three child guidance clinics have been established in Michigan in recent months as part of the program of the Michigan State Hospital Commission. Dr. Frank F. Tallman, Lansing, who was appointed director of mental hygiene of the commission last year, is in charge of the organization, supervision and coordination of the child guidance clinic system. The clinics are in Muskegon, Saginaw and Kalamazoo and requests have been made to the legislature for three similar clinics to be established July 1. The new clinics are a joint undertaking of the state and the community. The state pays all professional salaries for psychiatrists, psychiatric social workers and psychologists. The community provides office facilities, secretarial services, supplies and equipment. Each clinic has a local advisory committee which acts as a liaison body between the local clinic and the state hospital commission. Its chief responsibility is to raise an annual budget. Complete direction and control of the units rests with the state hospital commission. A similar clinic was opened in Lansing in 1938 and was made possible by a grant to the hospital commission from the Children's Fund of Michigan and contributions from the community. Each clinic will serve a territory within a radius of 60 miles. Consultative, diagnostic and therapeutic services are rendered by the clinic.

MINNESOTA

Special Society Election.—Dr. Paul G. Boman, Duluth, was named president of the Minnesota Society of Internal Medicine at its annual meeting in Duluth recently; Dr. Bayard T. Horton, Rochester, vice president, and Dr. Reuben A. Johnson, Minneapolis, secretary-treasurer.

Personal.—Dr. John deJ. Pemberton was reelected president of the Mayo Clinic staff at its recent annual dinner and Dr. Frank J. Heck was renamed secretary; both are in Rochester.—Dr. Russell R. Heim, Minneapolis, has been chosen coroner of Hennepin County.—Ralph W. Macy, Ph.D., professor of zoology at the College of St. Thomas, St. Paul, has been named professor of biology at Reed College, Portland, Ore.

MISSOURI

Collection on Ophthalmology.—The St. Louis Medical Society announces the gift of Dr. Joseph W. Charles, St. Louis, of a collection on ophthalmology. The group greatly augments the library's file on this specialty.

University News.—Dr. Karl F. Meyer, San Francisco, professor of bacteriology and director of the Hooper Foundation, University of California Medical School, delivered the Alpha Omega Alpha lecture, December 9, at Washington University School of Medicine, St. Louis, on "Plague."

Dr. Cook Heads Medical Department of Lambert Company.—Charles A. Cook, Ph.D., since 1931 research chemist at the Experimental Research Laboratories of Burroughs Wellcome and Company, Tuckahoe, N. Y., is now in charge of the department of medical and biologic chemistry at the Research Laboratories of the Lambert Pharmacal Company in St. Louis. Dr. Cook's work has been concerned with vitamins, chemistry of gastroenteric disease, amino acids and pituitary hormones.

Memorial Plaque Honors Dr. Coughlin.—Friends of the late Dr. William T. Coughlin presented a plaque to the St. Louis Medical Society, December 1, to serve as a memorial. The gift was made on the presentation of the first Robert James Terry Lecture, which was established under the will of Dr. Coughlin (THE JOURNAL, Nov. 28, 1942, p. 1049). The plaque was presented by Dr. Llewellyn Sale. Dr. Frederick E. Woodruff introduced the guest speaker, Dr. Stuart Mudd, Philadelphia, who gave the first Terry lecture on "Morphology of Pathogenic Bacteria and Viruses as Shown by the Electron Microscope with Some Practical Implications."

NEW JERSEY

Medical Scholarship Established.—Princeton University, Princeton, has received a legacy of $25,000 for the endowment of a scholarship to be awarded annually to "a man of outstanding scholarship, character and promise from the state of New Jersey, who intends to make the practice of medicine his life profession."

NEW YORK

Personal.—Dr. Simon A. King has been named health officer of North Dansville to succeed Dr. Alden J. Townsend, who resigned to enter military service.—A public celebration was held in Memorial Hall, Mineville, December 1, in honor of Dr. Thomas J. Cummins, who has completed twenty-five years of service in Moriah. An illuminated parchment scroll, a desk set and a $1,000 war bond were presented to Dr. Cummins.—Dr. Herbert M. Lyon, Buffalo, has been elected president of the board of trustees of Taylor University, Upland, Ind.; he graduated at the university in 1925.

New York City

Annual Contin Lecture.—Dr. Alfred Angrist, pathologist at Queens General Hospital, will deliver the annual Contin Lecture, January 22, on "The Mechanism of Brain Injury in Head Trauma." The lecture is sponsored by the Contin Society of the New York Medical College and Flower and Fifth Avenue Hospitals.

The Harvey Lecture.—Dr. Fuller Albright, assistant professor of medicine, Harvard Medical School, Boston, will deliver the fourth Harvey Society Lecture of the current series at the New York Academy of Medicine, January 21. His subject will be "Studies on the Pathological Physiology of Cushing's Syndrome."

Hospital Closed to Conserve Oil.—The Neponsit Beach Hospital for Children, Rockaway Beach, will be closed to "help the city make up its 10 per cent reduction in fuel oil allowance," newspapers reported January 4. Patients and hospital personnel were to be moved to other city institutions beginning January 5, it was stated. The hospital will be reopened when warm weather returns.

Personal.—Dr. Nathaniel Smith, former deputy medical superintendent of the Morrisania City Hospital, has been appointed medical superintendent of the Fordham Hospital.—Dr. Donald D. Van Slyke recently was elected an honorary member of the British Physiological Society.—Mr. Newman M. Biller, assistant director of the Montefiore Hospital for Chronic Diseases, has been appointed executive director of the Home for Aged and Infirm Hebrews. He will be succeeded at Montefiore Hospital on January 1 by Dr. Sigmund L. Friedman.

Lectures on Child Psychotherapy.—The Association for the Advancement of Psychotherapy announces a series of lectures on various aspects of child psychotherapy. The first session opened January 13 on "Juvenile Delinquency and Psychotherapy." On January 27 the subject will be "Children's Reaction to the War and Its Psychotherapy." Subsequent topics will be: February 10, "Adolescents in Need of Psychotherapy"; February 24, "Mental Hygiene in School and Psychotherapy"; March 10, "The Nutritional Basis of Mental Disorders in Children"; March 24, "Clinical Psychotherapy of the Child"; April 14, "Preschool Education and Psychotherapy"; April 28, "The Role of the Family in the Psychotherapy of the Child," and May 5, "Adult Psychotherapy and Child Psychotherapy." Speakers participating in the entire series are laymen and physicians interested in psychotherapy of the child.

Four Schools Offered for Social Hygiene.—The board of education has granted permission to the city department of health to use four schools to give preinduction training courses on Saturday mornings. The board of education had refused to include such a course in the regular curriculum (THE JOURNAL, Dec. 26, 1942, p. 1407). In a letter to the Health Commissioner Ernest L. Stebbins, John E. Wade, deputy superintendent of schools, wrote that, should the health officials decide to organize these classes, "the board of education will not identify itself in any way with your proposals and we will not be in any position to advertise the lectures to the students; we will make available premises to you as we would to any other organization, but you must undertake the enterprise as a project of the department of health wholly unrelated in any way to the Board of Education." The request for high school instruction in social hygiene was made by Dr. Stebbins because of a 20 per cent increase in venereal infection among boys and girls 15 to 19 years old. In granting permission to use the schools, the board stated that any legitimate organization had the right to use the schools on Saturday mornings provided the facilities were available.

OHIO

Changes in Health Officers.—Dr. Gregory J. Nordenbrock, St. Marys, has been appointed health commissioner for Shelby County, effective December 15; he succeeds Dr. Harry Wain, Sidney, who resigned to accept a similar position in Miami County.——Dr. Clifford J. Baldridge, health commissioner of the city of Hamilton and Butler County for twenty years, has resigned, effective January 1.

Medicine in the War.—A series of public health lectures opened at the Cleveland Health Museum, January 10, with a talk by Dr. Neil T. McDermott, Cleveland, on "War Nerves." The series is sponsored by the Academy of Medicine of Cleveland and other speakers in the group, all of Western Reserve University School of Medicine, Cleveland, are:

Dr. David K. Spitler, January 17, Controlling Epidemics.
Dr. Roscoe D. Leas, January 24, The Whys of Blood Banking.
Dr. Robert F. Parker, January 31, Combating Soldier's Health Hazards.
Dr. Harold D. Green, February 7, Body Behavior in Flying.
Enos B. Buchanan, Ch.E., February 14, Dispelling Modern Food Fallacies.

Citizens' Committee Named for Medical Plan.—A citizens' committee has been organized to act as sponsors for the Cleveland Medical Service Association prepayment plan, newspapers report. The Academy of Medicine of Cleveland recently issued a statement indicating that the plan is not a part of the academy's activities. The citizens' committee includes one hundred and twenty-seven "leaders in the community's public and professional life." Subscribers to the plan will be limited to single persons with an annual income of not more than $1,800 and heads of families of not more than $2,400. The Cleveland Hospital Service Association has agreed to handle sale of service contracts to the public, it was announced.

Health Information Hour Suspended.—A new service to the community, which was sponsored by the Cleveland Health Museum in the form of a "Health Information Hour" under the title "Tell Me Doctor," has been suspended during January and February. The service constituted the selection of a group of questions sent in by the public and answered by a board of experts composed of Drs. James A. Doull, Richard A. Bolt, John J. Thomas and Helen A. Hunscher, Ph.D., all of Cleveland. The questions covered all questions of general interest in the field of human biology, medical science, personal health and community hygiene. The ten best questions received a dollar war stamp. If the experts could not answer the question the inquirer received a book entitled "1680 Health Questions Answered" by Dr. William W. Bauer, Chicago, director, Bureau of Health Education, American Medical Association, and, in addition, three dollars in war stamps. The public was invited to attend the program. It is hoped to resume the feature in March.

Dr. Herrick Given Honorary Membership in Denison Foundation.—Charles Judson Herrick, Sc.D., emeritus professor of neurology, University of Chicago School of Medicine, Chicago, and now in retirement at Grand Rapids, Mich., was given the first honorary membership in the Denison University Research Foundation, Granville, in recognition of his years of service to Denison University as professor of zoology and for his achievements as a scientist in the field of neurology. Dr. Herrick also gave the first two lectures under the foundation to the Denison student body and the Denison Scientific Association. The Denison University Research Foundation was established by an anonymous donor in June 1942 "to promote, in close cooperation with Denison University or other institutions engaged in like activity, constructive research in the arts and sciences and in any and all fields normally associated with the activities of American colleges and universities; to provide inspiration and leadership to such selected persons as indicate a high type of scholastic endeavor, and who reflect special aptitudes in integrated projects that will contribute to human betterment. . . ."

TENNESSEE

Course in Internal Medicine.—Dr. Robert P. McCombs, Philadelphia, recently opened a ten week course in internal medicine for physicians in Chattanooga and Hamilton County under the auspices of the county medical society.

State Supreme Court Upholds Medical School Expulsions.—The power of the University of Tennessee College of Medicine, Memphis, to dismiss students found guilty by school authorities of stealing examination questions has been upheld by the Tennessee Supreme Court, newspapers reported December 13. Two of five students dismissed by the college in 1940 filed a petition in Chancery Court in Memphis charging that they were dismissed without a proper hearing and seeking reinstatement to the medical school.

TEXAS

Radiological Society Cancels Meeting.—The annual meeting of the Texas Radiological Society, which was to be held this month, has been canceled. Dr. Herman Klapproth, Sherman, is the secretary.

Physician's Portrait Presented to Medical School.—A portrait of the late Dr. Meyer Bodansky, who had been associated with the University of Texas Medical Branch, Galveston, from 1919 until his death in 1941, was presented to the school by the alumni association during the semicentennial graduation exercises, Dec. 18, 1942. Dr. Bodansky was born in Elizabetgrad, Russia, in 1896. He received his doctor of philosophy degree from Cornell University, Ithaca, N. Y., in 1923 and his doctor of medicine degree at the University of Chicago in 1935. Dr. Bodansky had been, since 1930, serving as professor of pathological chemistry. In 1932 he was visiting professor at the American University of Beirut, Syria. At the time of his death he was also director of the laboratories of the John Sealy Hospital.

GENERAL

Exchange Fellowship and Travel Grants Awards Suspended.—The U. S. Department of State announces that for the duration of the war the award of official scholarships, fellowships and travel or maintenance grants to students from the United States will be suspended. They will be resumed as soon as feasible. However, the award of fellowships and travel and maintenance grants to citizens of the other American republics for study in the United States will not be suspended or discontinued.

New Motion Picture on the Registered Nurse.—The American College of Surgeons sponsored the premiere of a new sound motion picture "R.N.—Serving All Mankind." A grant from the Becton Dickinson Foundation for the Extension of Scientific Knowledge in cooperation with numerous organizations made the picture possible. The film is suitable for showing by hospitals, nursing associations and all types of civic, service and educational organizations. It tells the story of two girls who choose nursing as a career.

Delivers Presidential Address Over the Radio.—Irving Langmuir, Sc.D., delivered his address as retiring president of the American Association for the Advancement of Science over the Columbia Broadcasting System, December 26, on "Science, Common Sense and Decency." The association postponed its meeting for the first time since the Civil War. Arthur H. Compton, Sc.D., president of the association, introduced Dr. Langmuir, speaking from Chicago. Dr. Langmuir spoke from Albany, N. Y. Watson Davis, director of Science Service, opened the program from Washington, D. C.

Special Society Election.—Dr. William T. Wootton, Hot Springs National Park, Ark., was named president-elect of the Southern Medical Association at its recent meeting in Richmond, Va., and Dr. Harvey F. Garrison, Jackson, Miss., was installed as president. Dr. Wyndham B. Blanton, Richmond, Va., was chosen vice president. The association's award for outstanding original work by one of its members went to Dr. Perrin H. Long, professor of preventive medicine, Johns Hopkins University School of Medicine, Baltimore, for his studies on the sulfonamides. The award was received for him by his associate Eleanor A. Bliss, Sc.D.

Priorities for "Life and Death" Emergencies in Airplane Travel.—Announcement has been made of a class number 5 priority to be granted when necessary for a "life saving" flight, under a cooperative program of all airlines. A physician en route to attend an emergency case will be granted the recently established priority as will a child en route to a hospital for an emergency operation of some unusual or critical nature. Persons en route to funerals and other instances, sometimes described as "death cases," will not be granted priority. The Regional Air Priorities Offices, which will extend this priority, may be reached through any local airline office.

Pharmaceutical Companies Merge.—The Winthrop Chemical Company has absorbed the Alba Pharmaceutical Company, both of New York, and has taken over Alba's assets, properties, trademark and good will. According to an announcement, although Alba ceases to exist, its research and manufacturing facilities in Rensselaer, N. Y., have been consolidated with those of the Winthrop Chemical Company and its marketing policies remain undisturbed. Dr. J. Mark Hiebert, medical director of Alba, will become assistant to Dr. Theodore G. Klumpp, president of the Winthrop group, and other Alba personnel will be absorbed. As a result of the

merger, Fairchild Brothers and Foster, a wholly owned subsidiary of Alba, has become a wholly owned subsidiary of Winthrop. The Alba Company was incorporated in New York on Aug. 30, 1935.

Federation of Experimental Societies Cancels Meeting.—The executive committee of the Federation of American Societies of Experimental Biology has voted to omit the meeting which was scheduled to be held in Cleveland April 6-10. This action applies only to the federation as such and does not cover any meetings which may be organized by the constituent societies, including the American Physiological Society, the American Society of Biological Chemists, the American Society for Pharmacology and Experimental Therapeutics, the American Society for Experimental Pathology, the American Institute of Nutrition and the American Society of Immunologists. According to *Science*, provision will be made for publication in the *Federation Proceedings* of abstracts of such papers as would have been offered for presentation if a federation meeting had been held or which may be offered for presentation at meetings of the constituent societies.

Grants for Research in Endocrinology.—It is announced that requests to the National Research Council Committee for Research in Endocrinology for aid during the fiscal period from July 1, 1943 to June 30, 1944 will be received until February 28. Application blanks may be obtained by addressing the Division of Medical Sciences, National Research Council, 2101 Constitution Avenue, Washington, D. C. In addition to a statement of the problem and research plan or program, the committee desires information regarding the proposed method of attack, the institutional support of the investigation and the uses to be made of the sum requested. No part of any grant may be used by the recipient institution for administrative expenses. Applications for aid of endocrine research on problems of sex in the narrower sense cannot be given favorable consideration, but the committee will consider support of studies on the effects of sex hormones on nonsexual function, for example, on metabolism.

CANADA

Personal.—Dr. William E. Gallie, professor of surgery and dean of the University of Toronto Faculty of Medicine, Toronto, has been elected to honorary fellowship in the Royal Society of Medicine.——Dr. Ada I. Wallace, medical health officer for Emerson and the rural municipalities of Franklin and Montcalm, was recently appointed first woman coroner in the history of Manitoba, it is reported.

University News.—The two separate health service departments for men and women in the University of Toronto, Ontario, have been combined this year to form the University Health Service with Lieut. Col. Richard W. I. Urquhart, Toronto, as director. Dr. Gwendolyn E. Mulock, Toronto, is assistant director in charge of the woman's division. The health service now provides annual physical examinations for all undergraduate students.

PUERTO RICO

Bureau of Health Education.—The health education office, created in 1940 as an annex to the office of the commissioner of health, Department of Health of Puerto Rico, San Juan, has been converted into a bureau and its name changed to Bureau of Health Education and Research, in accordance with a recent act of the Puerto Rican legislature. The *Puerto Rico Health Bulletin* states that, although the last word of the new title implies scientific investigations, the alterations in functions have not yet been defined either by law or administratively and there has been no provision whatever made to justify the change in name. The general objectives are to disseminate health information, to teach the underprivileged class in particular and the public at large how to take advantage of the services provided by the various agencies of the insular health department and to help in drafting technical instructions for the use of medical officers, nurses, social workers, sanitarians and other employees of the health department. Its main activities include the editing and publishing of the *Health Bulletin*, the general supervision of the library of the department of health and the general preparation and distribution of health material.

LATIN AMERICA

New South American Journals.—The *Revista Peruana de Pediatría*, the official organ of the Sociedad Perunana de Pediatría, made its first appearance with the June issue. The first issue contained original articles and reports of various general sessions of the Peruvian Society of Pediatrics and a section of medical news. Drs. Carlos J. Krumdieck and Julio Muñoz Puglisvich are the editor and assistant editor, respectively. The headquarters of the new journal which will be published every three months are Washington 914, Lima, Peru.——The *Anales Neuro-Psiquiátricos del Frenocomio de Mujeres de Bogotá*, Colombia, has recently appeared. Drs. Edmundo Tejada Rico and Luis Jaime Sánchez are the editor and assistant editor, respectively.

Death in Other Countries

Sir Norman Walker, formerly president of the Royal College of Physicians, Edinburgh, and of the General Medical Council, died, Nov. 7, 1942, in Midlothian, aged 81. Sir Norman graduated at the University of Edinburgh in 1884. After being appointed resident physician in 1885 at the Royal Infirmary, Edinburgh, he was assistant physician for diseases of the skin and later full physician in the skin department at the infirmary. He was a representative of Scotland for thirty-five years on the General Medical Council. He received the knighthood in 1928 following a study of medical education in the United States and India.

CORRECTION

Treatment of Phosphorus Burns.—In the abstract of Godding and Notten's article on the treatment of phosphorus burns in the current medical literature department of THE JOURNAL, July 25, 1942, page 1059, in the last line in the first column, the words "sodium carbonate" should have been "sodium bicarbonate."

Government Services

Government Manual for Professional Men

The fall-winter 1942 edition of the United States Government Manual is now available from the U. S. Information Center or the Superintendent of Documents, Washington, D. C., for one dollar, either in money order or check. The Division of Public Inquiries prepares and publishes the manual for the Office of War Information. The book contains seven hundred pages detailing the legislative powers, functions, location, names and titles of chief officials of all the government departments and agencies. It also contains organization charts, a list of current federal publications and an invaluable section on "abolished and transferred agencies and functions." It is fully indexed both by subject and by personnel and serves as a ready reference handbook.

Examination for Hospital Training in Dietetics

The Civil Service Commission has just announced a student dietitian examination to fill positions in the Army Medical Center, Washington, D. C. Sixteen female students will be enrolled in this position on or about September 1, and an additional sixteen six months later. The War Department offers a six month training course in hospital dietetics at the Army Medical Center to those desiring to become graduate dietitians. The students will receive subsistence and quarters and a small remuneration during the six month training period. At the end of the training, students are eligible to assignment to positions as apprentice dietitian for a six month period at a salary of $1,440 a year. Those who successfully complete this apprenticeship will be eligible for retention in the service in the position of staff dietitian at $1,800 a year. To qualify for the examination for student dietitian positions, applicants must have completed a full four year college course which included appropriate study in chemistry, biology, social sciences, education, nutrition and dietetics, and institutional management. Applications will be accepted from senior students who expect to complete the required course by Feb. 1, 1944. Provisional appointment may be made prior to completion of the course, but, before entrance on duty, proof of the completion of the course must be submitted directly to the War Department. There are no age limits for this examination. Applications must be in the office of the commission in Washington by January 9. The examination announcement giving full details may be consulted or obtained at first and second class postoffices (except in the cities where the civil service regional headquarters offices are located, where the forms must be obtained from the regional office) or from the commission's Washington, D. C., office. Applications are not desired from persons engaged in war work unless higher skills could be utilized in the new position. War Manpower Commission's restrictions on federal appointment of persons in critical occupations in specified areas are given in form 3989, posted in first and second class postoffices.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Dec. 11, 1942.

The Names of Drugs

The war has cut off the large supply of drugs normally imported from Germany, of which many are now manufactured in England. The question of names has arisen. The General Medical Council has published, on the recommendation of the British Pharmacopeia Commission, lists of approved names of the drugs produced by British manufacturers. The object is to recognize nonproprietary names which can be used freely by manufacturers and avoid the difficulties to physicians and pharmacists which arise from a number of names for the same drug. When any of the drugs for which names have been approved are admitted to the British Pharmacopeia, the approved name becomes the official title, but recognition of an approved name does not imply that the drug will be admitted. The Pharmacopeia Commission has formed an advisory committee on nomenclature to assist in the selection of approved names. Suggestions for suitable names are invited from manufacturers interested in the production of drugs for which they are required. The commission hopes that the approved names will be generally adopted and the use of other names avoided.

The commission has laid down the following guiding principles: 1. Names should preferably be free from any anatomic, physiologic, pathologic or therapeutic suggestion. This applies only to chemicals. Such suggestion cannot always be excluded in naming biologic products. 2. The accurate chemical name should be used if suitable. When it is unsuitable an attempt should be made to form a name by combining significant syllables from the chemical name and to include an indication of the potent element or constituent of a compound. Names should preferably not be of more than four syllables. 4. They should be distinctive in sound and spelling and not liable to be confused with others. 5. Names difficult to pronounce or remember should be avoided. 6. Addition of a terminal capital letter or number should be avoided. 7. Names in the current United States Pharmacopeia should be used either as principal titles or as synonyms. 8. Names in the British Pharmaceutical Codex or in New and Nonofficial Remedies should receive preferential consideration. 9. The following terminations should be used as far as possible: -ine for alkaloids and organic bases, -in for glucosides and neutral principles, -ol for alcohols and the phenol group, -al for aldehydes, -one for ketones and other substances containing the CO group, and -caine or -aine for local anesthetics.

Among the approved names already published are Amethocaine hydrochloride, Cyclobarbitone, Dienoestrol, Diodone, Diphenan, Dithranol, Ethisterone, Hexazole, Menaphthone, Meprochol, Mesulphen and Sulphacetamide.

Increase in Tuberculosis Produced by the War

The health of this nation has actually improved since the outbreak of war, but there are certain exceptions. The increase in tuberculosis observed in the last great war has been repeated. In his Malcolm Morris memorial lecture Sir Arthur MacNalty, former chief medical officer of the Ministry of Health, said that tuberculosis was an inevitable result of war conditions, which brought overcrowding, limitation of protective foods, shortage of hospital beds, increased hours of work and general war strain. The great efforts made during the years 1918-1938, which had lowered the mortality from tuberculosis, would be retarded by this second great war. Civilian deaths from tuberculosis in England and Wales had risen from 26,250 in 1939 to 28,669 in 1941.

Counter measures must be applied after the war, and for this purpose more specialists in tuberculosis, more nursing and domestic staff, and more beds will be required. The machinery of organization should be made ready now. Every tuberculous man and woman leaving the fighting services or war industry should be rehabilitated, that is, put in a position to earn a livelihood. He advocated a scheme on the lines of the Papworth Village Settlement as embodying the secret of the successful treatment of tuberculosis. One of the results of the evacuation policy due to the air raids had been to transfer considerable numbers of children from London and other cities, where most of the milk was sterilized by heat, to small urban or country districts, where practically all the milk was supplied raw. That was bound to cause a rise in nonpulmonary tuberculosis in children, and already signs of this were apparent. He urged people to boil their milk if they could not obtain it pasteurized.

Danger of Nurses Contracting Tuberculosis in Sanatoriums

In the House of Commons the minister of health was asked whether in view of the suggestion that girls should be compelled to take up sanatorium nursing and of the efforts now being made to increase the number of nurses in such sanatoriums he would investigate cases in which nurses had contracted tuberculosis in the discharge of their duties and were now maintained either by public funds or on a sum which did not permit adequate and proper care. He was also asked what steps were taken in his department to ensure the rehabilitation of nurses who contracted tuberculosis when nursing tuberculous patients; i. e., whether he was satisfied that sufficient financial provision was made for such a nurse to ensure adequate food and clothing and a room apart from the rest of the inmates of the house where she might be more or less segregated.

The minister, Mr. Ernest Brown, said in reply that he would call attention to the statement in a recent report of the Medical Research Council that expert opinion in this and other countries was that the risk of contracting tuberculosis from nursing tuberculous patients in sanatoriums is no greater than that involved in general hospital nursing. A nurse in a tuberculosis institution who contracts the disease is given every care and attention appropriate to her condition by the institution. Arrangements for the care and after-care, directed to restore working capacity, are an essential part of the tuberculosis service and apply to nurses as much as to any other person who suffers from tuberculosis.

Early Diagnosis of Pulmonary Tuberculosis by Mass Radiography

Sir Pendrill Varrier-Jones, the pioneer of village settlements and therapeutic occupation for the tuberculous, died in 1941. Under the presidency of Sir Harold Whittingham, director general of medical services of the Air Force, the first memorial lecture to Varrier-Jones was delivered by Wing Commander Traill. He said that except in a disappointingly small percentage of cases we were a long way from the diagnosis of early pulmonary tuberculosis. The disease now claimed half the total deaths from all causes between the ages of 15 and 24 years. The best possible tuberculosis service, with every modern equipment, had made no improvement toward earlier diagnosis in ten years and the extent of the disease at diagnosis was such that the majority of patients were unsuitable for modern treatment and few survived five years following discharge from a sanatorium. This state of affairs was due to the fact that it was only on the arrival of symptoms, and not always then, that the patient sought advice. In x-ray examination we have a method which can reverse all this. The physician can seek out the patient and not wait until the patient seeks him.

The lecturer then gave the results of mass radiography of 40,119 personnel in the Air Force, including the Women's

Auxiliary Service. The miniature film could weed the abnormal from the normal, but for ultimate diagnosis a large film and full clinical and pathologic examination were necessary. Notwithstanding the fact that these 40,119 persons had been examined and passed by national service boards some six to twelve months previously and that all the men had a stricter examination within the previous six months with a view to selection for special duties, the x-ray examination showed that 65 of these unusually "fit" subjects (2.2 per thousand) of the 30,130 men exhibited signs of active tuberculosis and 108 (3.6 per thousand) signs of inactive disease. For the 9,989 women the figures were worse: 38 (3.8 per thousand) had active and 56 (5.6 per thousand) inactive disease.

The figures showed that, among our supposedly healthy adolescent and young population between the ages of 18 and 24, 3 per thousand have unsuspected active tuberculosis and that more than 1 per thousand is a potential source of infection, because, unknown to himself, he has a positive sputum. The population at these ages is some 5 million, from which it follows that we have among us some 15,000 persons suffering from unsuspected tuberculosis.

Before any extension of mass radiography can take place, much preparatory work must be done because workers associated x-ray examination with disease and economic disaster. Legislation must protect them against loss of employment and reduced standards of life for themselves and their families.

Dermatology in the British Expeditionary Force in France

At the annual meeting of the British Association of Dermatology and Syphilology, Dr. J. T. Ingram, who was consultant dermatologist to the British Expeditionary Force in France, described his experiences. He was disappointed to find that dermatology in the army is a cloak of respectability for venereology, as syphilis does not account for more than 5 or 6 per cent of venereal disease in the army, and a dermatologist should not be asked to treat gonorrhea, which belongs to the urogenital surgeon. Though there were many branches of special medical and surgical practice—ophthalmology, otology, dentistry, pathology—there was no organization for dermatology or, for that matter, for venereal diseases. He blamed dermatologists to some extent for this. It is seventy years since Hutchinson showed what a considerable part dermatology should play in the medical curriculum, and yet its leaders are still content to allow it to remain a trifling decoration on the cloth of medicine instead of insisting on its being an essential fabric.

After conferences at general headquarters it was decided to deal with simple acute dermatoses (impetigo and scabies essentially), acute gonorrhea and the continuation treatment of syphilis in field ambulances. The diagnosis and preliminary treatment of syphilis and venereal sores were conducted at certain casualty clearing stations, where mobile pathologic laboratories and specialist personnel were established. The more difficult chronic and abnormal cases were sent to separate dermatologic and venereal units established at general hospitals at the base. The medical officers for the field ambulances were recruited by calling for volunteers. From these a number were chosen and given a week of intensive instruction at the base, where they handled a wealth of clinical material and conducted, under supervision, the investigations and technic required of them in the field ambulances. The result was that excellent work was done in them and much wastage of man power in the army was avoided. At the base it was arranged that certain general hospitals should house units for the treatment of dermatologic cases under skin specialists and that others should house venereal units under specialists in venereal disease. Patients who needed hospitalization for longer than twenty-eight days under conditions of static warfare and seven days under active warfare were evacuated to England.

Opposition to the New Regulations for the Compulsory Treatment of Venereal Diseases

The introduction of the compulsory treatment of venereal diseases, as a result of the war, was reported in a previous letter to THE JOURNAL. As was to be expected, the new regulation at once aroused opposition. Dr. Edith Summerskill, a medical member of Parliament, with other woman members has tabled a "prayer" for its annulment. They think that it will operate unfairly against women and will be ineffective. The minister of health received a deputation from the Association for Moral and Social Hygiene and representatives of women's organizations to discuss the new regulation.

A pamphlet entitled "Venereal Disease Still a Problem in the United States" has been sent to the editors of the medical journals anonymously. It begins by referring to the compulsion existing in many states that prospective mothers and applicants for marriage certificates must have serologic tests. It then says "Nevertheless, judging from an article by de Kruif published in the *Reader's Digest*, September 1942, page 10, the wiping out of venereal disease is just as much a problem as ever." Quotations on the dangers of antisyphilitic drugs from the *Lancet* follow.

New Photographic Method for Identifying Human Remains

The trial of a man aged 49 at the Central Criminal Court for the murder of his wife occurred recently. The skeleton of a woman was found under a paving stone of the cellar of a Baptist chapel adjoining premises where he worked as a fire watcher. The chapel was damaged in an air raid and the body was found by a demolition worker. A fire occurred in the cellar four days after the woman disappeared, on April 11, 1941. There were signs of burning on the left side of the remains. The question of identity offered difficulty. Dr. Keith Simpson, pathologist, gave evidence that in his view death took place a year or eighteen months before he saw the remains on July 18, 1942. Evidence in support of identification with the dead woman was given by Miss Mary Newman, who is in charge of the photographic department at Guy's Hospital. She took a number of photographs of the remains and also made a picture of a photograph of the missing woman and on this superimposed a photograph of the skull. Evidence of identity was also given by a dentist. The prisoner was convicted. This is only the second case in which this photographic method of identifying human remains has been used. The first was in the Ruxton murder case in 1936, when it was introduced by two Scottish professors.

Vitamins for Expectant Mothers and Young Children

Concentrated orange juice from the United States is now available for all children up to the age of 5 years, instead of 3 as heretofore. Cod liver oil compound was already available for children up to 5. Both products can now be obtained under the government scheme by expectant mothers during the last six months of pregnancy. But the minister of food states that only 24 per cent of the children eligible were getting cod liver oil, and only 26 per cent were getting orange juice. The Ministry of Health, including its dietitian, Dr. J. C. Drummond, has therefore made an appeal to all parents to see that their children regularly take orange juice and cod liver oil. They can be obtained at local food offices and at 7,500 centers at a very low cost. A bottle of cod liver oil compound which lasts about six weeks costs only 20 cents, and a bottle of orange juice, equal to a dozen oranges and sufficient for a fortnight, costs 10 cents. Those who cannot afford these charges can obtain both free.

BUENOS AIRES

(From Our Regular Correspondent)

Dec. 5, 1942.

Public Health in Bolivia

A decrease in the population and in the physical strength of the people who live in the eastern part of Bolivia has been observed for the last few years. A medical committee under the chairmanship of Dr. H. Kempsi, head of the Lucha Antiverminosa of the Ministry of Public Health, was appointed by the government to investigate the causes of this situation. Medical examinations were made on 5,178 persons. It was learned that 99 per cent of the population of the region had helminthiasis, especially ancylostomiasis, and many had tuberculosis or malaria, leprosy, gonorrhea or syphilis. The committee found that improving the sanitary conditions of the villages and educating these people are problems of great importance. In almost all villages the supply of water is either insufficient in quantity or not well cared for. The ignorance and lack of individual and collective care are obvious. A tree called higuerón, or ogé, which grows in large numbers near the Beni river, has antihelminthic powers. Also numerous plants from which pyrethrum is obtained have antihelminthic powers.

Antituberculosis Campaign in 1941

Dr. Alejandro A. Raimondi, director of the Municipal Center of Buenos Aires for a Campaign against Tuberculosis, has published a report of work done by the center in 1941. There were 2,708 deaths from tuberculosis in Buenos Aires in that year. Tuberculosis in the city has increased because of the number of patients from the provinces who come to the city. The routine practice of taking roentgenograms of children has resulted in finding early tuberculosis in nonsuspected children and also in preventing the spread of the disease. The roentgen examination of the chest of apparently normal persons gave good results. Tuberculosis was found in 5 cases (1.3 per cent) of a group of 384 students (who had a roentgen examination of the chest in the Instituto Municipal de Tuberculosis) and in 25 cases (3.02 per cent) in a group of 826 applicants for municipal positions.

Brief Items

In Argentina a law was recently passed which established an honorary committee to conduct a crusade against echinococcosis. The committee is formed of physicians and veterinarians. It depends on the Ministry of Agriculture and the National Department of Hygiene.

The Pan American members of the Instituto Internacional de Protección a la Infancia, with headquarters in Montevideo, met the last week of August in Montevideo. Dr. Gregorio Aráoz Alfaro, the Argentine representative of the council of the institute, was president of the reunion. Miss Elizabeth Shirley Enochs of Washington was the representative of the Children's Bureau of the United States.

The Asociación Congresos de Cirugía, comprising representatives of medicine and surgery in Bolivia, Brazil, Chile, Paraguay, Argentina and Uruguay, resolved to meet for the first Congress of Surgery in Buenos Aires. The Asociación Argentina de Cirugía gave the preference to the University of Santiago, the fourth centennial of the foundation of which is celebrated this year. The congress is to be held in Santiago on November 14-19 to discuss acute peritonitis, fractures of the humeral diaphysis and nontuberculous purulent pleurisies. The address of the headquarters of the general secretariat office of the association is Santa Fe 1171, Buenos Aires.

The Asociación Argentina de Dermatología y Sifilología recently held a meeting in Buenos Aires to celebrate the fiftieth anniversary of the foundation of the chair of dermatology in the Faculty of Medicine of Buenos Aires. Delegates from South American countries were present. It was recalled that Dr. Baldomero Sommer was the first regular professor of the chair, which he occupied until his death in 1918. Dr. Maximiliano Aberastury occupied the chair from 1918 to 1925, when he retired. Dr. Pedro L. Baliña has occupied the chair since 1925. During the meeting, dermatologic sections were held with the collaboration of the delegates from South American countries. The advisability of forming a Latin American federation for the study of dermatovenereologic diseases and also a committee for studies on massive arsenotherapy was emphasized.

The association emphasized the importance of intensifying the crusade against leprosy in Argentina. The association also voted to establish scholarships for the interchange of dermatosyphilologists who work in clinics in various countries of the American Hemisphere.

Personals

Dr. Juan P. Garrahan of Buenos Aires was appointed to the chair of pediatrics and puericulture at the Faculty of Medicine of Buenos Aires to fill the vacancy left by Dr. Mamerto Acuña, who retired, having reached the age limit. Dr. Garrahan is the author of "Medicina Infantil," of which more than seventeen thousand copies have been published. He has written books on tuberculosis in childhood, rickets and vitamin K and is the editor of the *Archivos Argentinos de Pediatría*.——Dr. Alfredo V. Di Ció won the Mariano R. Castex prize, which is given by the Academia Nacional de Medicina of Buenos Aires, and the premio al mejor trabajo, which is given by the Faculty of Medical Sciences of Buenos Aires, for his book "Enfermedades de las arterias periféricas."——Drs. Egidio S. Mazzei and Jorge M. Remolar won the "Doctor Luis Agote" prize for their book, "Estudio clínicorradiológico del enfisema pulomonar." Dr. Mazzei previously was awarded prizes of the Faculties of Medicine of París, Brazil and Buenos Aires for clinical studies on pneumothorax and primary bronchopulmonary tumors.——Dr. Frank Norman Wilson of the University of Michigan Medical School recently delivered lectures at the Faculty of Medicine of Buenos Aires and the National Academy of Medicine.——Dr. Fred H. Albee of New York accepted the invitation which Dr. Oscar Ivanissevich, head of the Instituto de Clínica Quirúrgica, extended to him to come to Buenos Aires for the inauguration of the ward of orthopedics of the institute, which is named the Dr. Albee ward.——Dr. José Arce, ex-dean of the Faculty of Medical Sciences of Buenos Aires, is in the United States visiting scientific centers to study the organization of centers of hemotherapy.

Marriages

SIDNEY RICHARD KALISKI, San Antonio, Texas, to Miss Sophie Faverman at Albuquerque, N. M., December 4.

HUBERT BENBURY HAYWOOD JR., Raleigh, N. C., to Miss Virginia Louise Allison of Richmond, Va., October 17.

FREDERICK SMITH DERR, Williamsport, Pa., to Miss Ethel Warring of Allenwood, in Tampa, Fla., September 15.

CLAUDE NASH HERNDON JR., Winston-Salem, N. C., to Miss Margaret Forester Caldwell of Greensboro, October 10.

JAMES FRANCIS ZAGARIA, St. Paul, to Miss Marie Filomena Scaletta at Kansas City, Mo., October 10.

HOWARD BAILEY WILLIAMS to Mrs. Betty Carlson Lide, both of Birmingham, Ala., in November.

PAUL W. VAN METRE to Mrs. Lucy Hinton, both of Rockwell City, Iowa, October 11.

VIVIAN ALLISON TENNEY to Mr. John Franklin Boyer, both of New York, November 29.

BEN A. DREIBRODT, San Antonio, Texas, to Rita Leghart of Pittsburgh, November 25.

BEATY LEE BASS, Lenoir, N. C., to Miss Patsy Smith of Winston-Salem recently.

Deaths

George Washington Crile ✠ world renowned surgeon, died, January 7, at the Cleveland Clinic, aged 78, of subacute bacterial endocarditis.

Dr. Crile was born in Chili, Ohio, Nov. 11, 1864. He graduated at Ohio Northern University and in 1887 at the University of Wooster Medical Department, Cleveland, now Western Reserve University School of Medicine. Early in his career Dr. Crile studied in Vienna, London and Paris. He served at Wooster University first as lecturer and demonstrator in histology and later as professor of physiology and professor of the principles and practice of surgery. He was professor of clinical surgery at Western Reserve University from 1900 to 1911 and professor of surgery from 1911 to 1924. He was also director of research at the Cleveland Clinic Foundation, of which in 1921 he was a cofounder.

Research conducted by Dr. Crile included the basic factors concerned in circulation, respiration, blood chemistry and the body's source of energy. He was perhaps first to make a direct blood transfusion, performed in 1905.

Dr. Crile was awarded the Alvarenga prize by the College of Physicians of Philadelphia in 1901, the Cartwright prize by Columbia University in 1897 and 1903, the Senn prize by the American Medical Association in 1898, the *American Medicine* medal for service to humanity in 1914, the National Institute Society Sciences medal in 1917 and the Trimble Lecture medal in 1921. In 1925 the Lannelongue International Medal of Surgery was presented to him by the Société internationale de chirurgie de Paris, in 1931 the Cleveland medal for public service and in 1940 the distinguished service gold key of the American Congress of Physical Therapy.

The memberships in scientific societies of Dr. Crile included among others the American Association of Anatomists, the American Association for the Advancement of Science, American Association for the Study of Goiter, American Physiological Society, American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Southern Surgical Association, Southern Medical Association, American Philosophical Society, American Association of Pathologists and Bacteriologists, Society of Clinical Surgery, Society of Experimental Biology and Medicine, National Institute of Social Sciences, National Research Council, Association for the Study of Internal Secretions, American Heart Association, American Medical Editors' Association, Ohio State Medical Association, Cleveland Academy of Medicine, Cleveland Medical Library Association and the Inter-State Postgraduate Medical Association of North America, of which he was chairman of the program committee. He was a member of the founders' group of the American Board of Surgery. In 1923 he served as president of the American Surgical Association.

A member of the board of regents of the American College of Surgeons since 1913, Dr. Crile was chairman of the board from 1917 to 1939 and president of the college in 1916. In 1907 he was Third Vice President of the American Medical Association and chairman of its Section on Surgery, 1910-1911. He was also an honorary or corresponding fellow or member of many American and European societies.

In 1898 Dr. Crile was brigade surgeon in the volunteers with the rank of major, serving in Cuba and Puerto Rico. He was a major in the Officers' Reserve Corps, and professional director of the U. S. Army Base Hospital number 4, Lakeside Unit (British Expeditionary Force number 9) in service in France for one year beginning May 1917, subsequently serving as senior consultant in surgical research, lieutenant colonel and in November 1918 colonel. He was brigadier general in the Medical Officers' Reserve Corps in 1921, holding the same rank in the auxiliary reserve corps since 1929. In 1919 he was awarded the Distinguished Service Medal and in the same year became an honorary member of the Military Division, third class, Companion of Bath (British). In 1922 he was made a Chevalier in the French Legion of Honor.

Dr. Crile was a prolific contributor to scientific literature. Among numerous articles and textbooks are Surgical Shock, 1897; Surgery of Respiratory System, 1899; Certain Problems Relating to Surgical Operations, 1901; On the Blood Pressure in Surgery, 1903; Hemorrhage and Transfusion, 1909; Anemia and Resuscitation, 1914; Anoci-Association (with Lower), 1914; second edition, Surgical Shock and the Shockless Operation Through Anoci-Association, 1920; Origin and Nature of the Emotions, 1915; A Mechanistic View of War and Peace, 1915; Man, an Adaptive Mechanism, 1916; the Kinetic Drive, 1916; the Fallacy of the German State Philosophy, 1918; A Physical Interpretation of Shock Exhaustion and Restoration, 1921; The Thyroid Gland (with others), 1922; Notes on Military Surgery, 1924; A Bipolar Theory of Living Processes, 1926; Problems in Surgery, 1928; Diagnosis and Treatment of Diseases of the Thyroid Gland (with others), 1932; Diseases Peculiar to Civilized Man, 1934; The Phenomena of Life, 1936; the Surgical Treatment of Hypertension, 1938, and Intelligence, Power and Personality, 1941.

Dr. Crile's contributions to experimental work through the years resulted in many improvements in surgery and medical practice. He traveled widely; his charm and his forceful personality marked him for leadership early in his career. The contributions of his active and curious mind are a lasting monument.

GEORGE WASHINGTON CRILE, M.D., 1864-1943

Jabez Henry Elliott, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1897; associate in medicine and clinical medicine at his alma mater from 1909 to 1931 and since then professor of the history of medicine; president of the American Association of the History of Medicine; member and past president of the American Clinical and Climatological Association; past president of the Canadian Association of Tuberculosis; fellow of the American College of Physicians and in 1923 vice president; fellow of the Ontario Medical Association and in 1904 vice president; fellow of the Academy of Medicine of Toronto and in 1920 president; fellow of the Royal College of Physicians of Canada, the College of Physicians and Surgeons of Ontario, the Ontario Historical Society and the British Medical Association; in 1934 was elected president of the Canadian Military Institute, which he served as librarian for many years; a founder of the National Tuberculosis Association; physician in charge of the Muskoka Cottage Sanatorium from 1898 to 1907; during World War I served in the medical corps of the Canadian Army; for many years chief of diseases of the chest at St. Michael's Hospital and associate physician at the Hospital for Sick Children; in 1900 went to Nigeria as a member of an expedition studying malaria and other diseases; Ontario representative on the editorial board of the *Canadian Medical Association Journal*; aged 69; died, December 18.

Ewing Wilber Day, Provincetown, Mass.; Georgetown University School of Medicine, Washington, D. C., 1889; member of the Medical Society of the State of Pennsylvania and the American Academy of Ophthalmology and Otolaryngology; member and past president of the American Otological Society, Inc.; member, president in 1908 and treasurer from 1901 to 1907 and from 1909 to 1937 of the American Laryngological, Rhinological and Otological Society; past president of the Allegheny County Medical Society; a founder and past president

of the Pittsburgh Academy of Medicine; fellow of the American College of Surgeons; for many years professor of otology, laryngology and rhinology at the University of Pittsburgh School of Medicine, where he had been professor emeritus since 1928; a founder of the Pittsburgh Eye and Ear Hospital and its chief of staff from 1908 to 1828; consultant, St. Margaret Memorial and Children's hospitals, Pittsburgh, and the Columbia Hospital, Wilkinsburg; specialist certified by the American Board of Otolaryngology; lieutenant colonel in the medical reserve corps of the U. S. Army not on active duty; served as a major and lieutenant colonel in the medical corps of the U. S. Army during World War I; aged 80; died, November 24, in the Doctors Hospital, New York.

Henry Erdmann Radasch, Philadelphia; Jefferson Medical College of Philadelphia, 1901; appointed professor of histology and embryology in the department of anatomy on Nov. 20, 1922 and on June 15, 1942 became emeritus professor of histology and embryology at his alma mater, where he had been demonstrator of histology and embryology from 1901 to 1903, associate from 1903 to 1918 and associate professor from 1918 to 1922; instructor of histology at the Pennsylvania College of Dental Surgery from 1906 to 1909 and adjunct professor of physiology, pathology and bacteriology, 1909-1910; instructor in anatomy at the Pennsylvania Academy of Fine Arts from 1913 to 1918; histologist at the Philadelphia General Hospital in 1920; member of the American Association of Anatomists; author of "Manual of Anatomy," "A Compend of Histology" and "A Manual of Histology"; contributed fifteen articles to the Reference Handbook of the Medical Sciences; aged 68; died, November 29, of coronary occlusion.

Alfred Baker Spalding, San Francisco; Columbia University College of Physicians and Surgeons, New York, 1900; appointed instructor in obstetrics at the University of California Medical School in 1902 and in 1909 professor of obstetrics; became professor of obstetrics and gynecology at the Stanford University School of Medicine in 1912 and in 1934 professor emeritus; member of the House of Delegates of the American Medical Association in 1917, 1919 and 1923; member of the California Medical Association, the Pacific Coast Surgical Association and of the Pacific Coast Society of Obstetrics and Gynecology; honorary fellow in 1933 of the American Gynecological Society; specialist certified by the American Board of Obstetrics and Gynecology, Inc.; director of San Francisco Maternity from 1904 to 1915; consultant in gynecology and obstetrics at San Francisco Hospital and Stanford University Hospitals until 1933; aged 68; died, November 26.

Albert Allemann, Takoma Park, Md.; George Washington University School of Medicine, Washington, D. C., 1904; retired at the end of February 1932 from active duty in the library of the Surgeon General's Office, where he had been since 1900; was for fifteen years principal assistant librarian and editor of the *Index Catalogue*; at one time assistant editor of the *Index Medicus* and later on the staff of the *Quarterly Cumulative Index Medicus*; will be remembered for his editing on the *Index Catalogue*, including four volumes of the second and all of the third series; aged 82; died, December 10.

Henry Willard Allen, Ridgefield, Conn.; Medico-Chirurgical College of Philadelphia, 1909; author of "Diseases of the Rectum"; aged 65; died recently.

Raymond C. Almy, Auburn, N. Y.; Syracuse University College of Medicine, 1908; member of the Medical Society of the State of New York; coroner of Cayuga County; aged 60; on the consulting staff and formerly president of staff of the Auburn City Hospital, where he died, November 29.

Marvin Armstrong, Merkel, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1892; member of the State Medical Association of Texas; for thirty-five years surgeon for the Missouri, Kansas and Texas Railroad; aged 76; died, November 27, in a hospital at Fort Worth of complications as the result of injuries received in a fall.

Robert Anderson Bennett, Riverdale, Md.; George Washington University School of Medicine, Washington, D. C., 1906; past president of the Prince Georges County Medical Society; for many years medical examiner for Prince Georges County and health officer for Riverdale; one of the founders and director of the Citizens Bank of Riverdale; aged 80; died, November 11.

Urban Clark Billingsley ✠ Hayward, Calif.; Cooper Medical College, San Francisco, 1904; aged 67; died, November 15.

Sigmund F. Braunfield, New York; Long Island College Hospital, Brooklyn, 1919; aged 51; died, November 22, in the Manhattan General Hospital of cerebral hemorrhage and thrombosis.

Bethea Portis Brindley, Danville, Ala.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1892; aged 87; died, November 29, in the Benevolent Society Hospital, Decatur, of pneumonia.

Sara Craig Buckley, Le Roy, N. Y.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1884; at one time a medical missionary in Japan; aged 84; died, November 24.

Luther Grow Bunker ✠ Waterville, Maine; Medical School of Maine, Portland, 1892; served twelve years as a member of the Board of Registration of Medicine in Maine; for six years served as city physician and as mayor in 1907 and 1908; in June 1942 was presented with a gold medal by the Maine Medical Association in recognition of his fifty years in the practice of medicine; aged 74; died, November 26.

Martin Francis Cashin, St. John's, Newfoundland, Canada; McGill University Faculty of Medicine, Montreal, Que., 1923; aged 43; died suddenly, November 5.

Oscar G. Cranford, Sasser, Ga.; Baltimore Medical College, 1892; member of the Medical Association of Georgia; aged 76; died, October 25, in a hospital at Moultrie.

Charles Clarence Davis ✠ Essex, Conn.; Yale University School of Medicine, New Haven, 1907; on the staff of the Middlesex Hospital, Middletown; aged 58; died, November 26, of carcinoma of the liver.

George Hicks Davis, Hollidays Cove, W. Va.; Baltimore Medical College, 1905; member of the West Virginia State Medical Association; aged 66; died, November 20, of cerebral hemorrhage.

Hervie Alden Dobson, Madison, Wis.; Columbian University Medical Department, Washington, D. C., 1876; Civil War veteran; aged 100; died, November 27.

Charles Russell Doyne, Albuquerque, N. M.; University of Arkansas School of Medicine, Little Rock, 1911; member of the New Mexico Medical Society; at one time on the staffs of the Southeastern Hospital for the Insane, Madison, Ind., the Longview State Hospital, Cincinnati, the Topeka (Kan.) State Hospital, the State Sanatorium for Tuberculosis, Norton, Kan., New Mexico State Hospital, Las Vegas, and the Arizona State Hospital, Phoenix; aged 54; was found dead, November 1, in a local hospital of a self-inflicted bullet wound.

William Casper Duke, Fredonia, N. Y.; Kentucky School of Medicine, Louisville, 1888; Jefferson Medical College of Philadelphia, 1893; for many years village health officer of Fredonia; aged 84; died, November 11.

Samuel Walker Ellsworth, Quincy, Mass.; Harvard Medical School, Boston, 1896; member of the Massachusetts Medical Society; served during World War I; had served on the staffs of Quincy City Hospital, the Massachusetts Memorial and the City hospitals, Boston; aged 72; died, November 26.

Richard Austin Flynn, Belleville, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1923; aged 44; died, October 8.

Bernard Freedman, Los Angeles; University of California Medical School, San Francisco, 1941; aged 26; died, October 8, of postoperative hemorrhage.

Roscoe S. Graves, Saco, Maine; Homeopathic Hospital College, Cleveland, 1883; aged 84; died, November 29, in the Trull Hospital, Biddeford, of chronic myocarditis, hypertension and uremia.

Oscar Blin Hall ✠ Warrensburg, Mo.; University Medical College of Kansas City, Mo., 1898; aged 74; died recently.

Orlando S. Harmon, De Kalb, Mo.; St. Louis College of Physicians and Surgeons, 1892; aged 78; died, November 6, in the Smithville (Mo.) Community Hospital.

Homer Benton Harper, Barberton, Ohio; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, Chicago, 1906; member of the Ohio State Medical Association; on the staff of the Citizens Hospital; aged 69; was instantly killed in an automobile accident, November 14.

Wayne Adelbert Harris ✠ Santa Ana, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; aged 61; died, November 25.

John Joseph Hayden, Worcester, Mass.; Baltimore Medical College, 1908; aged 62; died, November 26.

Fred Stanley Heimer, Unadilla, N. Y.; Baltimore Medical College, 1910; member of the Medical Society of the State of New York; formerly a pharmacist; for many years health

officer; served as a captain in the medical corps of the U. S. Army during World War I; aged 61; died, November 27.

Hiram A. Hess, Ross, Calif.; Barnes Medical College, St. Louis, 1897; aged 75; died, November 13.

Leander S. Holcomb, Riverside, Calif.; University of Louisville (Ky.) Medical Department, 1893; aged 77; died, October 4.

William Henry Hood, Reno, Nev.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1886; member of the Nevada State Medical Association; formerly surgeon for the Southern Pacific Railway; past president of the Pacific Association of Railway Surgeons; was a director of the Farmers and Merchants Bank; aged 80; died, November 29.

James Manney Howard Jr. ✠ Passed Assistant Surgeon, Lieutenant, U. S. Navy, retired, Kinston, N. C.; University of Virginia Department of Medicine, Charlottesville, 1915; entered the medical corps of the U. S. Navy May 22, 1917 and retired Feb. 15, 1922 for incapacity resulting from an incident of the service; served during World War I; aged 51; died, November 17, in the Parrott Memorial Hospital.

Edward Raymond Stone Jr., Washington, D. C.; Georgetown University School of Medicine, Washington, 1939; was commissioned a first lieutenant and later a captain in the Royal Army Medical Corps; aged 29; was killed in action in the Middle East, November 1, while in front line duty with the attacking forces during the advance in Egypt.

KILLED IN ACTION

CAPTAIN EDWARD R. STONE JR., ROYAL ARMY MEDICAL CORPS

Randall Hutchinson, Los Angeles; University of Pennsylvania Department of Medicine, Philadelphia, 1887; formerly professor of physical diagnosis at the University of Southern California College of Medicine; formerly served as a member of the consulting staff at the Children's Hospital; aged 82; died, November 12.

Clarence Andrew Kelly, St. Croix Falls, Wis.; Marquette University School of Medicine, Milwaukee, 1939; member of the State Medical Society of Wisconsin; on the staff of St. Croix Falls Hospital; aged 33; was accidentally killed while hunting deer on November 16.

Maud Emilie Taft Kew, Keene, N. H.; Woman's Medical College of Pennsylvania, Philadelphia, 1900; aged 68; died, November 7, in Boston.

Robert Bruce King, Newborough, Ont., Canada; Trinity Medical College, Toronto, 1893; died, October 17.

William Andrew Lee ✠ Fergus Falls, Minn.; Northwestern University Medical School, Chicago, 1911; past president of the Park Region District Medical Society; served overseas in the medical corps of the U. S. Army during World War I; served as health officer of Fergus Falls and coroner of Otter Tail County; aged 62; on the staff of St. Luke's Hospital; on the staff and formerly chief of staff of the George B. Wright Memorial Hospital, where he died, November 22, of uremia and pyelonephritis.

John McKiggan, Donkin, N. S., Canada; Dalhousie University Faculty of Medicine, Halifax, 1921; aged 51; died recently.

Robert Hopkin Paterson, Hamilton, Ont., Canada; University of Toronto Faculty of Medicine, Toronto, 1908; served as a captain in the Canadian Army Medical Corps during World War I; since 1920 had been in charge of special clinical work for the department of health with headquarters at the General Hospital; aged 59; died suddenly, November 6.

James William Prowell, Kansas, Okla.; St. Louis College of Physicians and Surgeons, 1896; county health physician for Delaware County; served as a first lieutenant in the medical corps of the U. S. Army during World War I; at one time associated with the Indian Service in White Horse, S. D.; aged 69; died, November 27, on state highway number 33, 2 miles East of Salina.

Ben L. Reitman, Chicago; American College of Medicine and Surgery, Chicago, 1904; at one time instructor of surgical pathology at his alma mater; author of "Second Oldest Profession: A Study of the Prostitute's Business Manager" and "Sister of the Road: The Autobiography of Boxcar Bertha"; a colorful figure in Chicago for many years; aged 63; died, November 16, of coronary thrombosis.

Winifred Brenda Reynolds, Stevensville, Mont.; Dalhousie University Faculty of Medicine, Halifax, N. S., Canada, 1900; aged 64; died, October 5.

George B. Ribble ✠ La Moure, N. D.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1904; past president of the Southern District Medical Society; aged 64; died, October 20, of cardiac thrombosis.

John Lewis Riggles, Washington, D. C.; Columbian University Medical Department, Washington, 1900; formerly associate clinical professor of obstetrics at the Georgetown University School of Medicine; at one time instructor in anatomy at his alma mater, known as the George Washington University School of Medicine; formerly dispensary physician at the Columbia Hospital for Women and had been in charge of the surgery dispensary at the George Washington University Hospital; aged 65; died, December 8.

Walter Alfred Sangster, Stouffville, Ont., Canada; University of Toronto Faculty of Medicine, 1889; aged 77; died, October 8.

Albert Lytleton Savage, Ventnor, N. J.; Jefferson Medical College of Philadelphia, 1887; aged 85; died, October 15, of chronic prostatitis and acute nephritis.

James C. Shanks, Toronto, Ont., Canada; McGill University Faculty of Medicine, Montreal, Que., 1881; aged 89; died, September 17.

Robert Lee Smith, Melbourne, Ark. (licensed in Arkansas in 1903); aged 66; died, November 17, of gout and uremia.

Roy James Snider, Thessalon, Ont., Canada; University of Toronto Faculty of Medicine, 1916; served during World War I with the Canadian Army Medical Corps as a lieutenant and later with the Royal Army Medical Corps as a captain; aged 50; died, September 20.

Joseph H. Spicer, Cumberland, Md.; Baltimore Medical College, 1910; aged 56; died, November 30, in the Memorial Hospital of chronic myocarditis.

Harry Stein ✠ Sandusky, Ohio; Syracuse University College of Medicine, 1930; aged 43; died, November 7.

Robert Mills Stephenson, Lexington, Miss.; Atlanta (Ga.) College of Physicians and Surgeons, 1908; member of the Mississippi State Medical Association; fellow of the American College of Surgeons; served during World War I; on the staff of the Holmes County Community Hospital; aged 59; died, November 20, of coronary thrombosis.

Arthur Ellis Threlkeld, Wheatley, Ky.; Chicago Homeopathic Medical College, 1886; member of the Kentucky State Medical Association; for many years chairman of the board of education of Wheatley, and bank president; aged 80; died, November 21, of coronary sclerosis.

William Massie Tunstall, Lovington, Va.; University of the City of New York Medical Department, New York; 1891; for many years chairman of the board of supervisors of Nelson County; aged 73; died, November 24.

Clarence David Vrooman, Ellenville, N. Y.; Albany Medical College, 1892; member of the Medical Society of the State of New York; aged 82; on the staff of Benedictine Hospital, Kingston, and of the Veterans Memorial Hospital, where he died, November 24.

William P. Watson, Dyersburg, Tenn.; Memphis (Tenn.) Hospital Medical College, 1899; member of the Tennessee State Medical Association; past president of the Dyer-Lake-Crockett Counties Medical Society; on the staff of the Baird-Brewer General Hospital; aged 68; died, November 18, of carcinoma of the sigmoid with metastasis.

Edward George Weadock, Lima, Ohio; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1900; member of the Ohio State Medical Association; served overseas in the medical corps of the U. S. Army during World War I; aged 66; died, November 22.

James A. Wright ✠ Morrison, Ill.; Beaumont Hospital Medical College, St. Louis, 1887; aged 83; died, November 18.

Correspondence

"VITAMINS FOR COLDS"

To the Editor:—In the article entitled "Vitamins for the Prevention of Colds" by Cowan, Diehl and Baker, on page 1268 in the Dec. 19, 1942 issue of THE JOURNAL, the following paragraph appeared: "Most of the studies for the prevention of colds have been limited to vitamin A alone or to vitamins A and D as contained in cod liver oil. The experiments with vitamin A have resulted almost uniformly in negative results, while cod liver oil has been reported by a number of authors to reduce the severity and by some the frequency of colds. Most of the latter reports, however, are based on inadequately controlled studies.[1]" Under footnote 1 appeared a reference to a paper by Drs. Alfred F. Hess, J. M. Lewis and L. H. Barenberg entitled "Does Our Dietary Require Vitamin A Supplement?" published in THE JOURNAL, Aug. 26, 1933, page 657.

The implication, therefore, is that we expressed the opinion that cod liver oil reduced the severity or the incidence of respiratory infections and also that our study was inadequately controlled. We wish to call attention to the fact that our study was grossly misinterpreted by the aforementioned authors as, first, we found that cod liver oil or products containing vitamin A had no effect on the incidence or severity of respiratory infections and, secondly, we had observed eighty infants who received no vitamin A supplements and served as controls. These control infants were housed in a model child caring institution in the same wards as those who received vitamin A supplements.

In a previous communication (Barenberg, L. H., and Lewis, J. M.: Relationship of Vitamin A to Respiratory Infections in Infants, THE JOURNAL, Jan. 16, 1932, p. 199) as well as in a subsequent report (Lewis, J. M., and Barenberg, L. H.: The Relationship of Vitamin A to the Health of Infants, *ibid.* April 23, 1938, p. 1338) we also found that the addition of vitamin A to the average diet of infants had no beneficial effect on the incidence or severity of respiratory infections.

J. M. LEWIS, M.D.
L. H. BARENBERG, M.D.
New York.

"THE PSYCHIATRIC ASPECTS OF MARIHUANA INTOXICATION"

To the Editor:—In the September 1942 issue of the *American Journal of Psychiatry* there appeared a paper entitled "The Psychiatric Aspects of Marihuana Intoxication" by Drs. Allentuck and Bowman. The paper contained certain observations which appear to be based on research conducted in New York City at Welfare Hospital under the auspices of the Mayor's Committee on Marihuana. In the Dec. 5, 1942 issue of THE JOURNAL there appeared an editorial on the paper by Drs. Allentuck and Bowman.

The research of Drs. Allentuck and Bowman was made, it is true, on only 77 subjects, and those apparently were all drawn from a prison population. Nevertheless, several of the conclusions reached confirmed information in our possession. Thus the indication that marihuana precipitates in certain persons psychoses and unstable and disorganized personality is in accord with findings already in our possession. The conclusions of the study, as Dr. Kolb points out in his remarks on the paper (printed at the end of Allentuck and Bowman's paper in the *American Journal of Psychiatry)* certainly make it clear that use of marihuana may be an important contributory cause to crime. Drs. Allentuck and Bowman state definitely that marihuana by relaxing inhibitions may permit antisocial tendencies to come to the fore.

Of course, the primary interest of the Bureau of Narcotics is in the enforcement aspect. From that point of view we feel that it is very unfortunate that Drs. Allentuck and Bowman should have stated so unqualifiedly that use of marihuana does not lead to physical, mental or moral degeneration and that no permanent deleterious effects from its continued use were observed. I am aware, of course, that the *American Journal of Psychiatry* and THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION are published for a select professional group of readers who will understand the statement for what it was, that is, a scientific statement that certain phenomena were not observed in the study of a small group drawn from a prison population. More undiscriminating readers are perhaps likely to interpret the statement as the final word of the medical profession. Also there may well be some unsavory persons engaged in the illicit marihuana trade who will make use of the statement in pushing their dangerous traffic.

I am sure that you and most of your readers are familiar with the studies which have led to the conclusions that continued use of marihuana produces, or is a contributing factor in, mental disorders and physical deterioration. I have collected and attach quotations from a few sources which discuss the problems that arise from the use of marihuana:

"The relationship between insanity and hemp drug addiction has been worked out by us in some of the large mental hospitals" (Chopra, R. N., and Chopra, G. S.: Present Position of Hemp Drug Addiction, memoir 31, Indian Medical Research Memoirs, supplementary series to *Indian Journal of Medical Research,* July 1939).

"There seems no doubt that cannabis is responsible for a proportion of the admissions to mental hospitals in the Union" (Watt. J. M., and Breyer-Brandwijk, Maria G.: The Dagga Problem in South Africa, *South African M. J.* **10:** 573 [Aug. 22] 1936).

"It is proved beyond doubt that the prolonged use of Indian hemp usually leads to insanity. . . . There is a special form of mental disease commonly met with in India which is produced by prolonged moderate use of hemp drugs in any form. . . . Prolonged use of large doses of hemp mixed with dhatura seeds is responsible to some extent for unpremeditated murder, running amok, grievous hurt, etc., which occur daily in a vast country like India" (Dhunjibhoy, J. E.: A Brief Résumé of the Types of Insanity Commonly Met with in India, with a Full Description of "Indian Hemp Insanity" Peculiar to the Country, *J. Ment. Sc.* **76:** 254 [April] 1930).

"Indian hemp plays an important role in the greater part of mental disorders observed in the Mussulmen of the Regency. . . . Chronic intoxication leads at length to insanity. . . . The abuse of cannabis leads to insanity. . . . Chronic (cannabis) intoxication is serious in that it leads at length to total loss of will power. Intellectual decadence is complete" (Brotteaux, Pascal: Hashish—Weed of Folly and Dreams, Paris, Véga, 1934).

"We have a number of instances where the hemp drug habit has been so established in relation to insanity that, admitting (as we must admit) that hemp drugs as intoxicants cause more or less of cerebral stimulation, it may be accepted as reasonably proved that hemp drugs do cause insanity" (Report of Indian Hemp Drugs Commission, 1893-1894).

"The drift toward a chronic condition is very gradual. The subject becomes less and less fit for work. An inveterate addict lives in a state of permanent stupor. Eventually he has to be placed under restraint as the result of some crime or at any rate of acts of violence. In serious cases of dementia due to hashish, mental and organic collapse go hand in hand" (League of Nations document O. C. 1542 [o], dated Geneva, Feb. 17, 1937, Subcommittee on Cannabis of the Advisory Committee on Traffic in Opium and Other Dangerous Drugs, Report by Dr. J. Bouquet, Hospital Pharmacist, Tunis, Inspector of Pharmacies, Tunis, containing answers to the questionnaire submitted to the experts, document O. C. 1542 [j]).

"In visits paid by the writer to the Cairo Insane Asylum, it was found that insanity was due to the inhalation of hashish by smoking" (Church, Archibald, and Peterson, Frederick: Nervous and Mental Diseases, Philadelphia, W. B. Saunders Company, 1908).

"Continued use of the drug causes insanity in many cases" (Kolb, Lawrence: Marihuana, *Federal Probation,* publication of the Bureau of Prisons, Department of Justice).

"When used daily in large quantities, the direct action on the cerebrum often causes chronic mental deterioration" (Yawger, N. S.: Marihuana—Our New Addiction Problem, *Am. J. M. Sc.* **195:** 351 [March] 1938).

"Hashish smoking gives rise to general physical deterioration." (Lewin, Louis: Phantastica, Narcotic and Stimulating Drugs: Their Use and Abuse, New York, E. P. Dutton & Co., 1931).

O'Shaughnessy, medical director of Bengal Army in 1838, reported at least twelve eventual evil consequences of indulgence in cannabis (O'Shaughnessy, W. B.: On the Preparations of Indian Hemp or Gunjah, London, 1838).

"In certain circumstances hashish delirium has been seen to persist for several days and to assume disturbing proportions" (Richet, Charles: Intellectual Poisons, Paris, 1877).

With respect to the possible therapeutic applications of marihuana, I strongly agree with Dr. Kolb that Dr. Allentuck and Dr. Bowman are there treading on exceedingly dangerous

ground. Certainly there is need of considerably more investigation before marihuana is used in attempted cures of morphine addicts. I take it from their paper that Drs. Allentuck and Bowman are fully aware of that need for further investigation.

H. J. ANSLINGER, Washington, D. C.
Commissioner of Narcotics.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

CHICAGO, Feb. 15-16, 1943. Sec., Council on Medical Education and Hospitals, Dr. H. G. Weiskotten, 535 North Dearborn Street, Chicago.

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, Jan. 9, page 148.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, Jan. 20-22 and March 1-3. Exec. Sec., Mr. Everett S. Elwood, 225 S. Fifteenth St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Chicago, Feb. 15-16. Sec., R. Glen Spurling, 404 Brown Bldg., Louisville, Ky.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I.* Various centers, Feb. 13. Candidates in military service may take Part I at their place of duty. *Oral. Part II.* Pittsburgh, May 19-25. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral. All Groups. Parts I and II.* March 1. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* New York, May or June. Final date for filing application is March 1. Sec., Dr. Dean M. Lierle, 1500 Medical Arts Bldg., Omaha, Neb.

AMERICAN BOARD OF PEDIATRICS: Starting July 1, 1943, Group I will be abolished. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF PSYCHIATRY & NEUROLOGY: Detroit, prior to the meeting of the American Psychiatric Association. Final date for filing application is March 1. Sec., Dr. Walter Freeman, 1028 Connecticut Ave., N.W., Washington, D. C.

AMERICAN BOARD OF SURGERY: Part I. March 4. Final date for filing application is Jan. 25. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: Chicago, Feb. 12-14. Sec., Dr. Gilbert J. Thomas, 1409 Willow St., Minneapolis.

Tennessee September Report

The Tennessee State Board of Medical Examiners reports the written examination for medical licensure held at Memphis, Sept. 30-Oct. 3, 1942. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Twenty-seven candidates were examined, 20 of whom passed and 7 failed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Georgetown University School of Medicine		(1938)	1
Howard University College of Medicine		(1942)	1
Northwestern University Medical School		(1941)	1
University of Tennessee College of Medicine		(1942, 16)	16
Vanderbilt University School of Medicine		(1942)	1

School	FAILED	Year Grad.	Number Failed
University of Tennessee College of Medicine		(1942, 7)	7

Fifteen physicians were licensed to practice medicine by endorsement from August 19 through November 12. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
University of Alabama School of Medicine		(1900)	Alabama
College of Medical Evangelists		(1941)	Pennsylvania, (1942) N.B.M.Ex.
Stanford University School of Medicine		(1935)	California
Emory University School of Medicine		(1932), (1940)	Georgia
University of Illinois College of Medicine		(1941)	Illinois
University of Louisville School of Medicine		(1928)	Kentucky
Tulane University of Louisiana School of Medicine		(1938)	Georgia
Duke University School of Medicine		(1935)	N.B.M.Ex.
University of Cincinnati College of Medicine		(1931)	Ohio
Western Reserve University School of Medicine		(1911)	Ohio
Hahnemann Medical College and Hospital of Philadelphia		(1921)	Penna.
University of Tennessee College of Medicine		(1942)	Mississippi
Medical College of Virginia		(1913)	Virginia

Arkansas November Report

The Arkansas State Board of Medical Examiners reports the written examination for medical licensure held at Little Rock, Nov. 5, 1942. The examination covered 12 subjects. An average of 75 per cent was required to pass. One candidate was examined and passed. The following school was represented:

School	PASSED	Year Grad.
University of Arkansas School of Medicine		(1941)

Five physicians were licensed to practice medicine by reciprocity from June 6 through Nov. 27, 1942. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Loyola University School of Medicine		(1942)	Illinois
Tulane University of Louisiana School of Medicine		(1931)	Louisiana
Johns Hopkins University School of Medicine		(1933)	Maryland
University of Tennessee College of Medicine		(1931), (1941)	Tennessee

Hawaii July Report

The Board of Medical Examiners of Hawaii reports the written examination for medical licensure held at Honolulu, July 13-16, 1942. The examination covered 10 subjects and included 80 questions. An average of 75 per cent was required to pass. Twelve candidates were examined, 10 of whom passed and 2 failed. Four physicians were licensed to practice medicine on endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
University of Southern California School of Medicine		(1942)	1
Loyola University School of Medicine		(1942)	1
Tufts College Medical School		(1941)	1
Creighton University School of Medicine		(1941)	1
New York University College of Medicine		(1937)	1
University of Rochester School of Medicine and Dentistry		(1931)	1
Hahnemann Medical College and Hospital of Philadelphia		(1939)	1
University of Pennsylvania School of Medicine		(1918), (1939)	2
University of Wisconsin Medical School		(1936)	1

School	FAILED	Year Grad.
Chicago Medical School		(1940)
Pennsylvania Medical School, Shanghai		(1936)

School	LICENSED BY ENDORSEMENT	Year Grad.
University of Colorado School of Medicine		(1939)
George Washington University School of Medicine		(1936)
Harvard Medical School		(1938)
Cornell University Medical College		(1933)

South Carolina June Report

The State Board of Medical Examiners of South Carolina reports the written examination for medical licensure held at Columbia, June 22-24, 1942. The examination covered 17 subjects and included 50 questions. An average of 75 per cent was required to pass. Forty-six candidates were examined, all of whom passed. Seven physicians were licensed to practice medicine by reciprocity and 1 physician so licensed on endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Emory University School of Medicine		(1942)	1
Tulane University of Louisiana School of Medicine		(1942, 4)	4
Jefferson Medical College of Philadelphia		(1942)	1
Medical College of the State of South Carolina		(1942, 40)	40

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Atlanta College of Physicians and Surgeons		(1905)	Georgia
University of Georgia School of Medicine		(1938), (1939)	Georgia
University of Louisville Medical Department		(1910)	Kentucky
New York Medical College and Flower Hospital		(1936)	Ohio
Duke University School of Medicine		(1937)	Penna.
University of Nashville Medical Department		(1902)	Texas

School	LICENSED BY ENDORSEMENT	Year Grad.
Boston University School of Medicine		(1939)

Rhode Island October Report

The Rhode Island Board of Examiners in medicine reports the written examination for medical licensure held at Providence, Oct. 1-2, 1942. The examination covered 10 subjects and included 73 questions. An average of 80 per cent was required to pass. Ten candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Tufts College Medical School	(1941),	(1941)*	2
St. Louis University School of Medicine	(1942)*		1
Syracuse University College of Medicine	(1921)		1
Jefferson Medical College of Philadelphia	(1940),	(1941, 2), (1942)*	4
University of Alberta Faculty of Medicine	(1936)		1
Dalhousie University Faculty of Medicine	(1942)*		1

* Licenses have not been issued.

Colorado October Report

The Colorado State Board of Medical Examiners reports the written examination for medical licensure held at Denver, Oct. 7-9, 1942. The examination covered 8 subjects and included 63 questions. An average of 75 per cent was required to pass. Four candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
University of Chicago, The School of Medicine	(1939)		1
Deutsche Universität Medizinische Fakultät, Prag	(1921)		1
Osteopaths *			2

* Examined in medicine and surgery.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Liability of Manufacturer or Distributor for Death Resulting from Inhalation of Carbon Tetrachloride Sold in Cans Not Labeled "Poison."—In the course of his employment over a period of about two months, McClaren used a liquid solvent, carbon tetrachloride, to remove grease from the inside of a boiler he was installing. On May 4, 1938 he worked from three to six hours inside the boiler's preheater, a cased in box about 14 feet long, 8 feet high and 40 inches wide, where the temperature was about 110 F. During that time the solvent was kept inside the preheater in an open pail, and the workman from time to time saturated a rag in the pail and "sloshed" it around the inside of the preheater. He became ill that day, just when the reported case does not state, and three days later died from carbon tetrachloride poisoning. Subsequently the administratrix of his estate brought suit for his death against the defendant, who had sold the carbon tetrachloride to the deceased's employer. From a judgment for the defendant, the administratrix appealed to the Supreme Court of Missouri, division No. 1.

The liability of the defendant was predicated on the negligent, so it was contended, failure of the defendant to label the containers in which the solvent was sold so as to indicate that the contents thereof were poisonous, in alleged violation of an Illinois statute, the state in which the deceased was working, which made it a criminal offense for a person to sell or deliver "any arsenic, strychnine, corrosive sublimate, prussic acid or other substance . . . usually denominated as poisonous, without having the word 'poison'" affixed to its labels. Apparently, it was conceded that if the defendant in marketing the solvent had violated this statute he was admittedly negligent, and there was a legal causation between his negligence and the death of the workman. While carbon tetrachloride was not specifically mentioned in the statute just referred to, the plaintiff contended that it was included within the phrase "other substance . . . usually denominated as poisonous." In construing this statute, said the Supreme Court, so as to determine whether or not the defendant was negligent we must resort to that familiar rule of construction known as the ejusdem generis rule. According to that rule, where a statute contains general words only, the general words must receive a general construction, but where the statute enumerates particular classes or things, followed by general words, the general words so used are to be construed as applicable only to things of the same general character as those which are specified. Thus, before the phrase "or other substance . . . usually denominated as poisonous" can be construed to include carbon tetrachloride, we must be able to say that it is like some one of the species and kinds of poisons expressly mentioned in the statute. It could not do this, for, in the court's opinion, carbon tetrachloride contains no single element of the various poisons enumerated by the statute. Obviously, carbon tetrachloride is not a drug but a grease solvent sold commercially as a cleaning fluid, and is not the same kind or class as the substances mentioned in the Illinois statute. The poisons there mentioned are of such character and universally so dispensed as to require a warning of their poisonous nature if taken internally in order to prevent a purchaser, or other person into whose hands the drug may come, from taking the same internally by mistake and to guard against overdoses of such as may be prescribed for medicinal purposes, either alone in minute quantities or as an ingredient of a medicinal preparation. It follows, therefore, that in the light of the penal nature of this statute carbon tetrachloride is not plainly or necessarily included among its provisions and it was not negligence for the defendant to sell carbon tetrachloride without having the word "poison" affixed on the label of the container. Nor do we think, continued the court, that the administratrix has adduced any substantial evidence that the defendant negligently sold and delivered carbon tetrachloride in containers bearing no warning that its use might cause sickness or death. It appeared from the evidence that the carbon tetrachloride used by the workman had been taken from cans labeled "Volatile Solvent, use with adequate ventilation. Avoid prolonged breathing of vapor." The evidence showed that there was no danger in using this product unless it was used in a confined, unventilated place. Furthermore, an agreed statement of facts showed that other manufacturers of carbon tetrachloride use a similar label; in fact, the label as used by the defendant had been adopted by manufacturers of this product and had been approved by the Surgeon General of the United States [sic] in 1934. "No one is held by the law to a higher degree of care than the average in the trade or business in which he is engaged." *Ketterer* v. *Armour & Co.*, 2 Cir., 247 F. 921, loc. cit. 931, L. R. A. 1918D, 798. A man, in conducting his business in the way that everybody else in a like business does, has measured up to the standard demanded by the law and has exercised the ordinary care of prudent men engaged in the business.

The court therefore affirmed the judgment of the trial court in favor of the defendant.—*McClaren v. G. S. Robins & Co., 162 S. W. (2d) 856 (Mo., 1942).*

Society Proceedings

COMING MEETINGS

Annual Congress on Medical Education and Licensure, Chicago, Feb. 15-16. Dr. H. G. Weiskotten, 535 North Dearborn St., Secretary.

American Academy of Orthopaedic Surgeons, Chicago, Jan. 17-21. Dr. Myron O. Henry, 825 Nicollet Ave., Minneapolis, Acting Secretary.

Clinical Orthopaedic Society, Chicago, Jan. 18-21. Dr. Myron O. Henry, 825 Nicollet Ave., Minneapolis, Secretary.

Middle Section, American Laryngological, Rhinological and Otological Society, Detroit, Jan. 20. Dr. Voss Harrell, 2539 Woodward Ave., Detroit, Chairman.

Southern Section, American Laryngological, Rhinological and Otological Society, Chattanooga, Tenn., Jan. 28. Dr. Francis B. Blackmar, 1301 Broadway, Columbus, Ohio, Chairman.

Western Section, American Laryngological, Rhinological and Otological Society, Portland, Ore., Jan. 31. Dr. Irving M. Lupton, 1020 S.W. Taylor St., Portland, Ore., Chairman.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1932 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American J. Digestive Diseases, Fort Wayne, Ind.

9:359-398 (Nov.) 1942

Treatment of Intestinal Disorders in Military Forces. L. C. Gatewood, Chicago.—p. 359.
Relationship of Hypothalamus to Large Bowel. D. Sheehan, New York.—p. 361.
Concerning Influence of Glucose on Response of Human Stomach to Test Meals. H. Shay, J. Gershon-Cohen, S. S. Fels and H. Siplet, Philadelphia.—p. 363.
Relationship Between Gastric Acidity and Calcium. F. C. Val Dez and J. Sendroy Jr., Chicago.—p. 367.
*Acid Factor in Duodenal Ulcer as Evaluated by Acidity and Neutralizing Ability in Duodenal Bulb. J. E. Berk, J. E. Thomas and M. E. Rehfuss, Philadelphia.—p. 371.
Relationship Between Gastroduodenal Motility Phases and Symptoms Associated with Duodenal Ulcer in the Human. T. L. Patterson and D. J. Sandweiss, Detroit.—p. 375.
Congenital Anomalies of Primary Midgut Loop. J. M. Miller and E. G. Wakefield, Rochester, Minn.—p. 383.
Effect of Hemicellulose Hydrogels on Character of Stool and Bowel Movement. R. Bauer, New York.—p. 387.
Gastrointestinal Section: Army General Hospital. A. A. Hall, Atlanta, Ga.—p. 389.
Infra-Red Photography of Abdominal Wall. E. Wayburn, San Francisco.—p. 392.
Amount of Fat in Blood After Meal as Estimated by Counting the Chylomicrons. R. R. Cooper and H. Lusk, Ann Arbor, Mich.—p. 395.
Complete Biliary Obstruction Complicating Duodenal Ulcer: Perforation of Ulcer Followed by Immediate Release of Obstruction. S. Levine and G. B. Gordon, Brooklyn.—p. 397.

Acid Factor in Duodenal Ulcer.—Berk, Thomas and Rehfuss studied the gastric and duodenal acidity of 7 dogs, 22 normal persons and 23 patients with duodenal ulcer. There were some nineteen thousand determinations of the gastric and duodenal contents simultaneously collected from areas just above (pars pylorica) and just below (duodenal bulb) the pylorus. They observed that the contents of the first part of the duodenum are endowed with a considerable capacity to neutralize, buffer and dilute gastric chyme which commonly exceeds the physiologic needs. Nevertheless, even in normal subjects the duodenal bulb is an acid area and free acid is not an abnormal observation. In patients with duodenal ulcer the neutralizing ability in the duodenal bulb is impaired but not wholly absent. Such patients appear to differ from normal persons in that the neutralizing capacity in the duodenal bulb and gastric hyperacidity are defective. The acidity of the contents of the duodenal bulb is largely determined by the type of food being digested and is only partially related to the degree of gastric acidity. The acidity in the stomach and duodenal bulb is not sharply parallel. None of the customary measures of gastric acidity reliably indicate the behavior of the effective acidity in the duodenal bulb at the same time. The usual oral therapeutic dose of antacids to patients with duodenal ulcer only slightly and transiently reduces the acidity of the contents of the first part of the duodenum; the reduction may be followed by a rebound increase. Neutralization of the contents of the duodenal bulb by fasting equals, and in some respects surpasses, that observed during digestion. This neutralization in normal man is exceeded by that in normal dogs. The acidity of the contents of the first part of the duodenum is generally insufficient to affect gastric motility significantly except in patients with duodenal ulcer. It may be a factor in stimulating pancreatic secretion.

Archives of Internal Medicine, Chicago

70:689-918 (Nov.) 1942

Incomplete Rupture of Aorta: Heretofore Unrecognized Stage of Dissecting Aneurysm and Cause of Cardiac Pain and Cardiac Murmurs. T. M. Peery, Washington, D. C.—p. 689.
*Control by Radium for Gastric Acidity. J. A. Jenkins and M. McGeorge, Dunedin, New Zealand.—p. 714.
*Use of Daily Fecal Output of Urobilinogen and Hemolytic Index in Measurement of Hemolysis. E. B. Miller, K. Singer and W. Dameshek, Boston.—p. 722.
Function of Separate Kidneys in Hypertensive Subjects. H. Chasis and J. Redish, New York.—p. 738.
Maintenance of Nitrogen Equilibrium by Intravenous Administration of Amino Acids: Clinical Studies. S. S. Altshuler, Detroit; Hilda M. Hensel, Monroe, Mich.; P. Hecht and R. Pursley, Eloise, Mich.—p. 749.
Production and Study of Cardiac Failure in Thiamine Deficient Pigeons. R. L. Swank and O. A. Bessey, Boston.—p. 763.
*Sulfonamide Compounds in Therapy of Bacterial Endocarditis: Comparison of In Vitro Inhibitory Effects and Bacteriostatic Activity. E. S. Orgain and Mary A. Poston, Durham, N. C.—p. 777.
*Anthrax: Review of Sixty Cases, with Report on Therapeutic Use of Sulfonamide Compounds. H. Gold, Chester, Pa.—p. 785.
Polymyositis: Report of Fatal Case. D. Goldman, Cincinnati.—p. 822.
Sodium *d*-Lactate Tolerance as Test of Hepatic Function. C. Cohn, New York.—p. 829.
Syphilis: Review of Recent Literature. F. W. Reynolds, C. F. Mohr and J. E. Moore, Baltimore.—p. 836.

Radium for Gastric Acidity.—The effects of radium irradiation on the acidity of the gastric mucosa were studied by Jenkins and McGeorge. Fourteen patients with duodenal ulcer were treated with radium. In all, thirty tests of gastric function were carried out prior to radium treatment and forty-four after treatment. Thirteen of the 14 patients have had a decided reduction in acidity of the gastric juice and in the volume of juice secreted. Clinical improvement usually accompanied the chemical improvement.

Hemolysis.—Miller, Singer and Dameshek determined the "hemolytic index" from an average of the output of urobilinogen in the feces in four days. This determination has proved of great value in the diagnosis and follow-up of various blood dyscrasias, particularly those associated with increased blood destruction. Since the daily fecal output of urobilinogen depends on the total mass of circulating hemoglobin, it is important to relate the former to the latter. This is done in the "hemolytic index," which shows that 11.1 to 20.8 mg. of fecal urobilinogen is normally derived from 100 Gm. of circulating hemoglobin in twenty-four hours. In anemia, or of a small surface area (as in children), the hemolytic index may show a greatly increased rate of blood destruction, although the absolute content of urobilinogen may be normal. This is particularly evident in certain types of hemolytic anemia and in pernicious anemia; in the latter a normal level of bilirubin in the blood with a greatly increased hemolytic index is common. The various indexes (acholuric jaundice, "indirect" bilirubinemia, an increase in urinary excretion of urobilinogen, anemia and leukocytosis) of possibly increased hemolysis are not specific, but an increase in the fecal output of urobilinogen or in the hemolytic index is unequivocal evidence of an increased breakdown of blood.

Bacterial Endocarditis.—The in vitro inhibitory effects of seven sulfonamide compounds on twenty organisms isolated from 17 patients suffering from bacterial endocarditis were correlated by Orgain and Poston with the clinical bacteriostatic activity of these drugs in a series of thirty-three clinical (in vivo) experiments. A certain degree of correlation existed between the in vitro inhibitory effects of these drugs and their clinical bacteriostatic activity. This emphasizes the importance of preliminary in vitro experiments to determine the most effective drug against the freshly isolated organism and its possible clinical level of inhibitory action. It appears that the in vitro and the in vivo effects of the sulfonamides may be correlative.

Anthrax.—Gold's experience with the treatment of 60 cases of external anthrax since the advent of sulfonamide compounds leads him to believe that these compounds are reliable and safe substitutes for serum and also that the drugs should be given preference. Fifty-one of his patients were employees of a local mill engaged in the manufacture of inner lining for which the basic raw material is goat hair imported from China and India. The other 9 patients lived close to the mill and had contact with the employees or the mill's products. Twenty-one patients

were treated with antianthrax serum; 1 died. To secure recovery, 200 to 2,200 cc. of serum was administered intravenously. Neoarsphenamine, in addition to the serum, was of little or no benefit. Forty-two patients were treated with sulfonamides; 39 had excellent results; 1 patient became worse after intensive treatment with sulfapyridine and its sodium salt but recovered after large doses of antianthrax serum, neoarsphenamine and immunotransfusions; 1 failed to respond to adequate doses of sulfathiazole but recovered on serum therapy, and 1 was taken off the drug too soon and was given antianthrax serum instead, with good results. Sulfapyridine was the most effective sulfonamide compound; next came sulfathiazole, then sulfadiazine. Since nausea and vomiting are frequent with sulfapyridine, sulfathiazole is the drug of choice at present. Large doses of sulfathiazole should be given until edema is controlled. If there is no response in three days, antianthrax serum should be used. The use of sulfonamide compounds materially shortens hospitalization and disability.

Archives of Surgery, Chicago

45:691-862 (Nov.) 1942

Prothrombin and Hepatic Function. J. G. Allen and O. C. Julian, Chicago.—p. 691.
Benign Tumors of Stomach. G. S. Dudley, L. Miscall and S. F. Morse, New York.—p. 702.
Cysts of Pancreas. J. Rabinovitch and B. Pines, Brooklyn.—p. 727.
*Postoperative Chylothorax: Sudden Death Following Infusion of Aspirated Chyle. B. B. Whitcomb and W. B. Scoville, Hartford, Conn. —p. 747.
*Sodium Salts of Sulfonamide Compounds: Study with Special Reference to Their Local Use in Wounds. C. L. Fox Jr., New York. —p. 754.
Treatment of Large Gastric Ulcers: Résumé of Ten Year Study. F. Steigmann, Chicago.—p. 764.
Relation of Serum Protein to Well Healed and to Disrupted Wounds. H. Koster and L. P. Kasman, Brooklyn.—p. 776.
New Methods for Determining Viability of Bowel: Preliminary Report with Clinical Cases. J. O. Herrlin Jr., S. T. Glasser and K. Lange, New York.—p. 785.
Progress in Orthopedic Surgery for 1941: Review Prepared by Editorial Board of American Academy of Orthopedic Surgeons.—p. 792.

Postoperative Chylothorax.—A case of postoperative chylothorax is reported as the result of inadvertent section of the thoracic duct during a sympathectomy for hypertension. Sudden death occurred after intravenous administration of autogenous chyle. This, Whitcomb and Scoville state, is the first time in their experience, as well as in the voluminous literature on the subject, that the thoracic duct was exposed and inadvertently torn during a sympathectomy for hypertension. The patient's extreme emaciation made her vulnerable. Delayed chylothorax occurred even though the thoracic duct had been doubly closed with four silver clips. The pressure of chyle within this duct is probably far greater than experimental work shows. The patient died promptly from what appeared to be anaphylactic shock. Necropsy was not permitted, and without it it is impossible to differentiate conclusively between anaphylaxis, fat embolism and a foreign protein reaction. Of the 6 cases reported in the literature in which infusion of autogenous chyle was instituted, 3 were fatal. Necessary precautions in the future should consist of a careful test for sensitivity followed by 5 to 10 cc. of chyle intravenously with a delay of thirty minutes before the infusion proper is started, rejection of specimens containing globules more than 3 microns in diameter and a twenty-four hour culture of the chyle. If chyle fails to meet the aforementioned standards, plasma and emulsified fats, with daily aspiration of the chyle, should be used instead. If chylothorax persists after one week of this regimen, phrenicectomy is indicated. Fat and protein should be infused early to prevent rapidly progressive emaciation.

Sodium Salts of Sulfonamide Compounds.—Fox demonstrated in dogs and mice that sodium salts of sulfathiazole and sulfadiazine are suitable for local use in wounds. To obtain more complete comparative data he determined the dissociation constants of sulfonamide compounds. It is noteworthy that in the body sulfathiazole and sulfadiazine are almost completely ionized, whereas sulfanilamide is but slightly ionized. The important fact is that since sulfadiazine and sulfathiazole occur in the body largely in the ionized form and since their sodium salts are only moderately alkaline, resembling sodium bicarbonate, their local use seems worthy of trial. The experiments show that oral, local, peritoneal and clysis administration of sulfadiazine give similar blood levels. Therefore a given quantity of drug suitably administered by any of these routes is distributed similarly throughout the body. The major advantages of local therapy are an immediate high concentration of the drug in the involved area. This concentration is sustained for twenty-four to forty-eight or more hours while the implanted drug is being transferred continuously but completely from the limited local area into the general circulation. A relatively gradual attainment (and loss) of a maximal blood level occurs. Since the implanted drug is removed completely when a soluble derivative is used, foreign body reaction at the local site does not occur. As sulfathiazole and sulfadiazine are extensively ionized at the p_H of the blood and when ionized their solubility is vastly increased over that in water or any of the more common solvents, it is suggested that fluid or semifluid preparations, including ointments, should be prepared from the sodium salts in aqueous and not oily bases if high local drug concentrations are desired. Safe renal excretion would be insured by favoring sulfonamide salt formation by keeping the urine alkaline.

Bulletin New York Academy of Medicine, New York

18:705-772 (Nov.) 1942

Marihuana. R. Adams, Champaign, Ill.—p. 705.
Lymphatic Participation in Cutaneous Phenomena. P. D. McMaster, New York.—p. 731.

Delaware State Medical Journal, Wilmington

14:207-222 (Oct.) 1942

Values. W. Marshall Jr., Milford.—p. 207.
The Transition. R. H. Lowe, New York.—p. 210.

Iowa State Medical Society Journal, Des Moines

32:483-532 (Nov.) 1942

Certain Peculiarities of Gallstone Disease. R. Fitz, Boston.—p. 483.
Symptoms of Pulmonary Disease. L. J. Galinsky, Oakdale.—p. 491.
Unilateral Exophthalmos Caused by Arteriovenous Aneurysm. J. C. Cunningham, Dubuque.—p. 495.
Factors in Lowering Mortality of Perforative Appendicitis. A. A. Eggleston, Burlington.—p. 497.
Practical Applications of Prenatal and Postnatal Care. C. W. Seibert, Waterloo.—p. 501.
Fatality from Acute Alcoholic Poisoning Complicated by Extreme Cerebral Edema: Report of Case. E. S. Brewster, Boone.—p. 504.
Laboratory and Clinical Findings of Pancreatic Diseases. M. G. Meyer, Marshalltown.—p. 506.

Journal of Clinical Investigation, Boston

21:651-810 (Nov.) 1942. **Partial Index**

Reactivity of Intact Blood Vessels of Fingers and Toes to Sensory Stimuli in Normal Resting Adults, in Patients with Hypertension and in Senile Subjects. G. E. Burch, A. E. Cohn and C. Neumann, New York.—p. 655.
Blood Flow in Hand and Forearm After Paravertebral Block of Sympathetic Ganglions: Evidence Against Sympathetic Vasodilator Nerves in Extremities of Man. J. V. Warren, C. W. Walter, J. Romano and E. A. Stead Jr., Boston.—p. 665.
Effects on Renal Resistance to Blood Flow of Renin, Angiotonin, Pitressin and Atropine, Hypertension and Toxemia of Pregnancy. H. Lamport, New York.—p. 685.
Capillary Blood Pressure in Man: Direct Measurements in Digits During Induced Vasoconstriction. L. W. Eichna and R. W. Wilkins, Baltimore.—p. 697.
Influence of Alterations in Acid-Base Balance on Transfers of Carbon Dioxide and Bicarbonate in Man. J. D. Rosenbaum, New Haven, Conn.—p. 735.
Effect of Muscular Exercise on Peripheral Circulation in Patients with Valvular Heart Disease. D. I. Abramson, S. M. Fierst and K. Flachs, Cincinnati.—p. 747.
Relation of Hippuric Acid Excretion to Volume of Urine. T. E. Machella, J. D. Helm and F. W. Chornock, Philadelphia.—p. 763.
Serum Iodine Fractions in Hyperthyroidism. E. B. Man, A. E. Smirnow, E. F. Gildea and J. P. Peters, New Haven, Conn.—p. 773.
Serum Magnesium in Thyroid Disease. R. F. Dine and P. H. Lavietes, New Haven, Conn.—p. 781.
Intubation Studies of Human Small Intestine: XXIII. Method of Determining Digestive Activity in Any Portion of Gastrointestinal Tract, with Some Measurements of Protein Digestion in Stomach and Small Intestine. K. A. Elsom, F. W. Chornock and F. G. Dickey, Philadelphia.—p. 795.

Maine Medical Association Journal, Portland

33:221-242 (Oct.) 1942

Cancer of Stomach. A. G. Brailey, Brookline, Mass.—p. 229.

33:243-262 (Nov.) 1942

Work of the Bingham Associates Fund in Maine. J. H. Pratt, Boston. —p. 243.

*Simple Efficient Splint for First Aid Care of Injured Arm or Leg. A. H. Parcher, Ellsworth.—p. 250.

Simple Splint for Arm or Leg.—Parcher describes the use of a board as a splint for the arm or leg when other splints are not available. The splint is made of plywood ⅜ inch thick and 3½ inches wide, with an expanded head end. The splint consists of three sections 12, 24 and 36 inches in length, respectively. The two shorter sections are for the arm, the longest one for the leg. The splint has double slots and bolts with wing nuts as a means for adjusting it quickly and firmly to different lengths and angles. The slots of the 12 inch section put across the slots of the longer 24 inch section and bolted permit adjustment for arm length. The broad headed end serves for fixation, as a spreader for traction, to prevent rotation of the extremity and for contact with the patient. To stabilize the splint, fixation bands from holes in the head end cross over the shoulder and are tied under the opposite shoulder.

Southern Medical Journal, Birmingham, Ala.

35:959-1050 (Nov.) 1942

*Carcinoma of Cervix: Clinical Evaluation of Radium Dosage and Supplementary Roentgen Irradiation Based on Study of 915 Cases. H. W. Jones Jr., Baltimore.—p. 959.

*Observations on Results of Combined Fever and X-Ray Therapy in Treatment of Malignancy. H. S. Shoulders, E. L. Turner and L. D. Scott, Nashville, Tenn.—p. 966.

Diagnosis, Treatment and Prognosis of Carcinoma of Buccal Mucosa. L. H. Jorstad, St. Louis.—p. 970.

Virus Pneumonia. H. T. Engelhardt and C. J. W. Wilen, New Orleans. —p. 973.

Id. S. S. Riven, Nashville, Tenn., and E. A. Stern, Rochester, N. Y. —p. 976.

Tuberculosis in 1942. C. H. Holmes, Atlanta, Ga.—p. 981.

Role of Bronchial Tree in Pathogenesis of Pulmonary Tuberculosis. B. L. Brock, Waverly Hills, Ky.—p. 984.

Spontaneous Mediastinal Emphysema: Summary and Report of Case. E. M. Meek, Huntington, W. Va.—p. 990.

Control of Pellagra. W. DeKleine, Washington, D. C.—p. 992.

Melanosis Coli: Review of Typical Case. J. H. Dodson, Mobile, Ala. —p. 996.

Hockey Stick Incision for Removal of Coccyx. G. T. Tyler Jr., Greenville, S. C.—p. 998.

Effect of Anesthesia on Chemotherapy with Derivatives of Sulfonic Acid. J. Adriani and Cornelia St. Romain, New Orleans.—p. 999.

Sulfathiazole Therapy in Venereal Disease. A. A. Creecy, Newport News, Va., and H. L. Switkes, Kecoughton, Va.—p. 1003.

*Preoperative Use of Sulfathiazole for Prevention of Postoperative Complications. J. A. C. Colston and R. W. Satterthwaite, Baltimore. —p. 1006.

Cutaneous Reactions Due to Sulfanilamide. R. W. Fowlkes, A. Pepple, Richmond, Va., and E. W. Waughan, Greensboro, N. C.—p. 1015.

Carcinoma of Cervix.—The data from 915 proved cases of carcinoma of the cervix treated at the Kelly Clinic between October 1927 and January 1936 are presented by Jones, who especially correlates the clinical stage of the disease, irradiation dosage and curability. A detailed analysis of the results discloses, as have studies by others, that the clinical stage of the disease is of paramount importance in determining the prognosis. The study of the effect of dosage on prognosis indicates that with a technic using large amounts of radium it is exceedingly dangerous to give less than 3,000 millicurie hours. The same tendency is evident from an analysis of the cases according to the clinical stage of the disease. Radium is administered by the broken dose technic usually at intervals of four weeks, a total dose of about 4,000 millicurie hours being administered. This dosage is applicable only with applicators and specific amounts of radon and cannot be compared with other methods. The broken dose technic is used because it aids in reducing preexisting cervical infections in the same way as preradium roentgen therapy, with the additional advantage that the cutaneous area available for irradiation is used for treatment directed primarily to the parametrium and iliac gland areas. Also there is a lessened incidence of troublesome proctitis with the broken dose method. The x-ray beam is directed toward the parametrium and iliac gland region of the side in question and not toward the midline. Pubic, sacral, trochanteric and perineal ports are employed, and sometimes even two small ports for each of these areas. A dosage of 1,500 to 2,000 roentgens, measured with scattering, is given to each port. Therapy must not be withheld even in the absence of palpable disease of the parametrium. Sulfanilamide and sulfathiazole have been used locally to reduce cervical infection. Whether their use will improve salvage remains to be seen, but they have been most helpful for combating infection.

Pyrexia and Roentgen Therapy.—On the basis of gradually accumulating evidence, Shoulders and his co-workers suggest that the maximal destructive effect of roentgen therapy on tumor cells should be obtained by applying it at the time of the greatest physiologic disturbance caused by induced fever, which is also lethal to certain tumor cells. They subjected 50 patients with far advanced inoperable cancer to roentgen therapy while the hyperpyrexia was at its height. Once the desired elevation of temperature (104 to 106 F.) is reached it is maintained for an hour. The patient, fully protected by blankets, is then transferred to a warm roentgen therapy room. The patient is kept well wrapped except for the portion of the body to be irradiated. The number of combined fever and roentgen treatments varied from one to four, depending on the lesion and its location. Additional roentgen therapy alone has been administered to all patients. There have been no fatalities traceable to the technic used. Thirty-nine (78 per cent) of the patients have shown definite improvement, such as relief of pain, decrease in the size of the tumor, cessation of hemorrhage, improved appetite and general comfort. The last in some instances suggests complete clinical relief. Eleven patients have shown no demonstrable improvement. The combined method of treatment produced results definitely superior to those obtained with irradiation alone. It is yet too early to indicate whether combined fever and roentgen therapy will be more than a palliative procedure. The procedure might serve as a more valuable adjunct to surgery than irradiation alone in cases in which postoperative irradiation is indicated.

Preoperative Use of Sulfathiazole.—Since July 1940 Colston and Satterthwaite have administered one of the sulfonamide drugs for varying intervals of time preoperatively to every patient with infection of the urinary tract at the first examination or at operation if opening of the urinary tract was contemplated. The incidence of postoperative complications and morbidity appeared definitely reduced. A critical comparison of the postoperative course of patients so treated preoperatively and a control nontreated series, but having similar operations, was undertaken. Of 110 treated preoperatively, 39 had a temperature of 100 F. or more on the first postoperative day, in 20 it was 100.5 F. or more, in 14, 101 F. or more and in 3 it was 102 F. or more. In the control group 87 of 196 had a temperature of 100 F. or more; 57, 100.5 F. or more; 40, 101 F. or more; 14, 102 F. or more, and 7, 102.5 or more. On the second, third and fourth postoperative days the difference in the temperature of the two groups was essentially the same. Practically the same difference in respiratory infection and other postoperative morbidity existed in the treated and nontreated patients. There were no cases of pneumonia or bacteremia in the treated group as compared to 5 and 4, respectively, among the control patients.

Southern Surgeon, Atlanta, Ga.

11:755-808 (Nov.) 1942

Injuries of Spinal Cord and Cauda Equina. C. Pilcher, Nashville, Tenn. —p. 755.

Sterilization of Sulfonamides for Local Use: Neglected Problem. D. Lindsey, New Orleans.—p. 765.

Massive Gastrointestinal Hemorrhage Concomitant with Cholecystitis. E. G. Laird, A. M. Gehret and L. J. Rigney, Wilmington, Del.—p. 769.

Diagnostic Curettage. R. B. Greenblatt, Augusta, Ga.—p. 775.

Lobectomy for Suppurative Disease of Lung. R. A. Daniel Jr., Nashville, Tenn.—p. 780.

Latrodectus Mactans (Black Widow Spider) Bite as Surgical Problem. K. H. Aynesworth, Waco, Texas.—p. 788.

Safety Valve Anastomosis and Decompression in Intestinal Surgery by Use of T Tube. G. L. Carrington, Burlington, N. C.—p. 794.

Lateral Migration of Appendectomy Incision: Its Relationship to Mortality. R. E. Strain, Nashville, Tenn.—p. 797.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

49:453-580 (Oct.) 1942

*Some Factors in Prognosis in Carcinoma of Cervix. A. A. Gemmell. —p. 457.
Degenerative Vulvovaginitis Associated with Estrogen Imbalance. E. Shute.—p. 482.
*Erythroblastosis or Congenital Syphilis? Observations on Erythroblastosis and Its Differential Diagnosis from Congenital Syphilis. J. L. Henderson.—p. 499.
Contribution to Etiology of Toxemic Syndrome of Pregnancy. K. Blond. —p. 512.
Treatment of Disproportion Associated with Moderate or Slight Degree of Pelvic Contraction in Primiparas: Comparison Between Results Obtained by Instrumental Induction of Premature Labor and Method of Trial Labor. Vivian H. Barnett.—p. 524.
Vitamin E in Habitual Abortion and Habitual Miscarriage. E. Shute. —p. 534.
Pregnancy Following Intrauterine Application of Radium. Mary H. Mayeur.—p. 542.
Clinical and Biochemical Findings in Delayed Chloroform Poisoning. M. D. Crawford.—p. 549.

Prognosis in Carcinoma of Cervix.—Gemmell treated 151 patients with carcinoma of the cervix between 1929 and 1938. In all but 2 the diagnosis was confirmed microscopically. In only 1 patient was Wertheim's hysterectomy performed; the rest were given radium and high voltage roentgen therapy. The technic of applying radium was that advocated by Heyman. All the patients were followed up to December 1940 or to the date of their death. Only 40 patients were alive at this time. More serious appearances in the bladder were associated with the more extensive stages of the disease. The survival rates of patients with transverse ridging or edema was roughly half that of patients with no changes or only minor changes in the bladder. The growth of the cancer toward the rectum is of serious prognostic import and affords some information of life expectancy. Variation of the dose of radium did not seem to affect the prognosis. Microscopic classification of the growth from the examination of material obtained by biopsy was of no assistance in determining prognosis. Patients who had a low value for the Bendien test before treatment usually had a significantly lower survival rate than those whose value was in the normal zone. The age of the patient or the number of children that she had at the time of treatment was no guide to the prognosis. The duration of symptoms prior to treatment was of no prognostic value. The prognosis in true stump carcinoma was approximately the same as when the whole uterus was intact. The prognosis was not affected when the disease appeared within two years of a pregnancy.

Erythroblastosis or Congenital Syphilis.—During the last five years Henderson has encountered 53 infants with erythroblastosis. Nineteen of them recovered, 24 died and 10 were stillborn. In the present series 16 of the 46 mothers had 2, and 4 had 3 affected infants. First infants are seldom affected but, once the disease has appeared in a family, any subsequent infants are likely to be affected. There are four types of the disease: anemia hemolytica neonatorum, icterus gravis, hydrops fetalis and hepatic cirrhosis with intrauterine death and maceration. The fourth type is the worst type of erythroblastosis, although it seems to have escaped general recognition owing to the difficulties of obtaining macerated fetuses for examination. It seems probable that such fetuses with some edema have often been classified as having hydrops fetalis. Hydramnios during the last few weeks of pregnancy is common in this form of erythroblastosis, and intrauterine death is followed within a week or two by the delivery of a severely macerated fetus, and the pale pink placenta is greatly enlarged, as in hydrops fetalis. There is little or no edema. The liver is slightly, if at all, enlarged and it is usually greenish brown; it is much less diffluent than is expected from the degree of maceration. In syphilis the placenta is also pale pink with increased thickness and weight, but infarction, which is not a feature in erythroblastosis, is usually found in addition. In the placenta of this type of erythroblastosis a layer of Langhans' cells persists. This is the most characteristic microscopic feature. These cells normally disappear by the twenty-fourth week of pregnancy, and their persistence to term is not known to occur in any other disease. The spleen is greatly enlarged. It is important to recognize this type of erythroblastosis and to differentiate it from congenital syphilis, which it superficially resembles. The records of 4 such cases are given.

Lancet, London

2:445-474 (Oct. 17) 1942

*Fate of Transfused Plasma. J. Beattie.—p. 445.
*Peripheral Vasoneuropathy After Chilling: "Immersion Foot and Immersion Hand." C. C. Ungley and W. Blackwood.—p. 447.
Infectious Mononucleosis. L. Kilham and A. J. Steigman.—p. 452.
Sterilization of Sulfonamides. J. E. McCartney and R. Cruickshank.—p. 454.

Fate of Transfused Plasma.—Beattie states that when plasma or serum transfusion is given normal human beings or experimental animals the pretransfusion blood volume is restored, rapidly in some subjects and less rapidly in others. Transfusion of plasma with a normal plasma protein concentration after severe hemorrhage does not necessarily restore the blood volume to the normal value, even when the quantity of the plasma transfused is equal to or exceeds the total volume of blood lost. The increase in protein reserves which plasma transfusions bring about may be almost as important as the increase in blood volume. The drain on these reserves in severe infections and after extensive burns is obviously great; to support them may be as valuable as to combat bacterial invasion by sulfonamides. In shock the rate of plasma protein replacement is slow, but as the plasma volume is increased the rate of replacement also increases. Movement of fluid into the blood stream takes place at rates, in man, of the order of 200 cc. an hour. At the same time plasma proteins can enter at the average rates of about 15 Gm. an hour. Such rates soon after hemorrhage may conceivably be much higher. On the other hand, after transfusion fluid may leave the blood stream at rates of 100 cc. a minute and plasma proteins at 4 to 6 Gm. a minute. It is by no means clear how these massive movements are effected without ill results. The study shows that there is yet much to learn of the mechanisms involved in the control of plasma volume and mass movements of plasma protein.

Peripheral Vasoneuropathy After Chilling.—Ungley and Blackwood give an account of 80 cases of "immersion foot and hand" encountered in two and a half years in Scotland. The exposure or rather immersion lasted up to fourteen days. They suggest that the term "immersion foot" is inaccurate and inadequate, as it does not include both the causative factor—cold—and the resulting neural and vascular disturbance; i. e., a peripheral vasoneuropathy after chilling. Judging from the patients' histories, the following factors appear to influence the occurrence and the severity of the vasoneuropathy: time of exposure, temperature of water, immobility, body cooling, seasickness, starvation, age, race (the dark skinned races were more prone than the northern races), morale and treatment on rescue. The footwear afforded some protection during short exposure, but boots constricted the swelling feet and impaired the circulation during long exposure. There was no evidence that previous susceptibility to cold feet or chilblains was predisposing. Biopsy of interdigital nerves from two feet amputated two and a half and four months after exposure and of two lower limbs amputated four and eleven months after rescue showed almost complete wallerian degeneration of the interdigital nerves and no significant vascular change. The tissues of the amputated limbs showed a persisting edema. The main nerve trunks showed severe degeneration and early regeneration; in the larger arteries there was slight intimal and medial fibrosis, in the large veins (1 case) patchy organized recanalized thrombi. The small vessels were not significantly abnormal. The muscles showed degenerative changes more severe than those following denervation. Probably injudicious warming of the affected limbs after rescue accentuates the damage by raising the metabolic demands of the tissues while they are still ischemic. For some hours after rescue, affected limbs should be kept cool while the patients' bodies are being warmed. Once cold and wet have penetrated, boots should be discarded before they become tight. Active movements and postures impeding circulation should be avoided. Once rescued, a man is stripped of wet clothing in a cool room and wrapped in blankets with the hands and feet exposed, and

he is given hot drinks. Massage is contraindicated. Patients are kept in bed, sometimes for many weeks; early walking may cause excoriation, blistering or increased swelling. The feet are raised on pillows, exposed to the air and kept dry. Sulfanilamide powder may be applied to wounds and blisters. Beneficial results from "dry cooling" the hot hyperemic limbs with fans or ice bags are reported from Canada.

2:475-502 (Oct. 24) 1942

War and the Advancement of Social Medicine. W. Jameson.—p. 475.
Trypanosomiasis Treated with "Pentamidine." T. L. Lawson.—p. 480.
*Febrile Reactions Among Smallpox Contacts. W. Napier and Alice M. Insh.—p. 483.
Toxic Blood Level of Sulfanilamide from Local Application. R. A. Gordon and V. H. Bowers.—p. 484.
Perforated Peptic Ulcer in Wartime. I. D. Riley.—p. 485.

Febrile Reactions Among Smallpox Contacts.—Febrile reactions occurred in 40 of 92 contacts received at a reception house for contacts during an outbreak of variola major in Glasgow. Of the 92 persons 22 were men, 28 women and 42 children less than 14 years of age. Fifty of the contacts had had close association with a smallpox patient for three to eight days, 27 had less intimate exposure, and the contact of 15 was limited to one or two occasions. All contacts were vaccinated on the day of admission to the reception house, with success in 43; 29 who showed little or no response after several days were revaccinated successfully, and 20 were resistant to the vaccinia virus. A second vaccination appeared to activate the earlier one, which until then had shown no activity. The febrile reactions during the period of quarantine of 30 were clearly due to vaccinia and 2 to variola; 8 presented some difficulty in diagnosis. The onset of pyrexia varied between the sixth and thirteenth days after vaccination. Its duration was from one to three days. From a study of the fever of the 8 patients in whom it was difficult to classify, Napier and Insh conclude that: 1. Smallpox may not be easy to recognize even in known contacts under constant observation. 2. Careful discrimination is required to decide whether the febrile attacks in contacts are due to vaccinia or to variola. 3. In a person who was recently vaccinated vaccinia is the most likely cause when the eruption is sparse, but a few typical spots may be sufficient to indicate variola with certainty. 4. When vaccinia can be ruled out, a short febrile illness, with or without transient spots, that occurs in the second week after exposure offers presumptive evidence of variola.

Medical Journal of Australia, Sydney

2:253-282 (Sept. 19) 1942

Normal Heart and Conditions Simulating Cardiac Disease. E. H. Stokes.—p. 253.
Investigation of Effect of Administration of Vitamin B_1 on Gastric Secretion and Motor Activities of Stomach: Preliminary Report. Barbara Wood, Beryl Splatt and I. Maxwell.—p. 263.
School Children's Teeth. Marjorie Casley Smith.—p. 269.

Tubercle, London

23:171-194 (Aug.) 1942

Prevention of Tuberculosis: Outline of New Scheme and Analysis of Economic Factor. J. E. Stokes.—p. 171.
Simple Sputum Concentration Method for Demonstration of Tubercle Bacilli E. Nassau.—p. 179.

Schweizerische medizinische Wochenschrift, Basel

72:533-556 (May 16) 1942. **Partial Index**

Question as to What Extent Medical Practitioner Can Contribute to Success of Operation Before and After Hospitalization. H. Heusser.—p. 533.
Knaus-Ogino Method of Birth Control and Its Value. A. Labhardt.—p. 537.
*New Method of Stimulating Gonadotropic Function of Pituitary. M. Julesz.—p. 541.
Clinical Control of Effects of Liver Extracts. E. Jéquier-Doge.—p. 544.
Association of Aurantiasis Palmaris, Acanthosis Nigricans and Epidermodysplasia Verruciformis in Case of Gastric Cancer. H. Jeanneret.—p. 547.

New Method of Stimulating Gonadotropic Function of Pituitary.—Barborka made the observation that 30 per cent of women who received a ketogenic diet acquired amenorrhea. Although Barborka remedied this condition by the administration of vitamin B_1, Julesz is convinced that a hormone rather than a vitamin is involved, because Hoffmann and Anselmino were able to isolate from the anterior lobe of the hypophysis a substance which increased the ketone bodies in the blood and was designated as the ketogenic hormone or the hormone of the fat metabolism. It is probable that the anterior pituitary plays a part in the development of ketosis and that in response to a ketogenic diet it elaborates the ketogenic hormone in increased quantities. The author investigated the question of whether ketosis stimulates only this or also other pituitary functions in mice and in human subjects. On the basis of his observations he considers it highly probable that ketosis stimulates the anterior pituitary to an increased production of the follicle stimulating principle and that any stimulus that is exerted on the anterior pituitary is probably also extended to the entire lobe. The author cites examples which indicate that the functions of the anterior pituitary do not change in an isolated manner. The ketogenic diet greatly stimulates the ketogenic hormone production, but it also stimulates the gonadotropic hormone production. With the exception of roentgen rays, the ketogenic diet is the only means of stimulating the anterior pituitary. In view of the fact that it increases the production of the follicle stimulating principle it is theoretically indicated in cases in which the gametokinetic function is to be increased. Thus it could be used in certain cases of azoospermia and in cases of hypofunction of the anterior pituitary such as hypophysial dwarfism and infantilism and incipient Simmonds' disease. The ketogenic diet could be used for diagnostic and prognostic purposes.

72:557-580 (May 23) 1942. **Partial Index**

Sex Hormone Therapy in Gynecology and Obstetrics. R. Wenner.—p. 557.
Age Incidence Principle of Investigation in Evaluating Biologic Significance of Inherited Variations in Problems of Human Constitution: Types of Scapula. W. W. Graves.—p. 561.
True and Supposed Danger of Infection in Diathermic Puncture of Corpus Ciliare for Glaucoma: Question Whether Secretion of Aqueous Humor Can Be Reduced by Diathermic Puncture of Ciliary Body. Anna Ernst.—p. 565.
*Trombidiosis (Harvest Itch): New Focus in Switzerland. R. Schuppli.—p. 568.

Trombidiosis: New Focus in Switzerland.—Schuppli reports that in July 1941 trombidiosis was observed for the first time in the region around Basel, Switzerland. A number of soldiers exhibited a severely itching exanthem in the axillas, on the articular flexor surfaces and about the hips. All the men who acquired the exanthem had picked bush beans. Investigation revealed red mites on the clothing and body of persons returning from the bean fields, and the same mites were discovered on the bean plants. They were identified as Trombicula autumnalis, or Leptus autumnalis. It is the larval form of the mite which causes the exanthem. The eruption is found on the covered parts of the body, particularly where the clothing adheres tightly. Shortly after a larva has attached itself to the skin, a red spot appears and becomes urticarial. An intensely itching papule develops which may have a small vesicle. Scratching ruptures the vesicles, and crusts form. The scratching may result in secondary infection and pyoderma. The itching is extremely severe, intensified attacks occurring during the night. The papules persist for from ten to fourteen days. Two of about 100 soldiers were apparently immune and remained free from the exanthem in spite of exposure. The sudden appearance of trombidiosis in a region formerly free from it may be due to the introduction of the soy bean into this region. The treatment of trombidiosis is of minor importance, since it subsides spontaneously in about ten days. The itching can be counteracted by a menthol or zinc preparation. As a prophylactic measure the author suggests that the mites could be destroyed chemically while they are in the soil during the winter, or that the plants could be sprayed with insecticides. For the individual prophylaxis American authors recommend the use of sulfur on clothing and body. The author suggests application of a zinc preparation to the sites predisposed to attacks by the mites. Shower baths with generous soaping and change of clothing immediately after exposure may also prove helpful.

Anales del Hosp. de Niños e Inst. de Puericult., Rosario

1-230, 1941. **Partial Index**

*Dick's Reaction in Scarlet Fever. A. Invaldi.—p. 127.
Infarct of Spermatic Cord. Case in Infant. A. Biejer and A. Colombo. —p. 149.

Dick's Reaction in Scarlet Fever.—Invaldi performed Dick's test on 150 children from 1 to 13 years of age with scarlet fever. The injection of toxin was systematically repeated with intervals of seven days. The test gave negative results in 113 of 141 patients who were brought to the hospital in the course of the first week of the disease, in 4 of 5 patients who entered the hospital in the second week and in the 4 patients who were brought to the hospital on the third and four weeks of the disease. The author concludes that, according to his observations, the rate of negative results is 80 per cent. A negative reaction early at the beginning of the disease is negative all through it. Positive results of the reaction change to negative results in the third week of the disease in 50 per cent of the cases. Age, sex and complications of scarlet fever do not have any influence on the results of the reaction.

Revista Medica de Chile, Santiago

70:477-568 (July) 1942. **Partial Index**

Dietetic Treatment in Hepatic Cirrhosis. A. Mardones Acosta and H. Dooner.—p. 479.
Origin of Hyperbilirubinemia and Fecal Pleiochromia in Pernicious Anemia. H. Alessandri, Ducci and R. Etcheverry.—p. 484.
Autotransfusion in Ruptured Ectopic Pregnancy and Other Considerations. H. Reyes.—p. 489.
*Pellagra in Adults in Santiago de Chile: Review of 110 Cases. H. Alessandri, P. Garcia Palazuelos and J. Lerner M.—p. 498.
A Year of Experience with Electropyrexia. M. Figueroa Echaiz-Vidal. —p. 508.
*Thrombopenic Purpura Caused by Sulfanilamides. M. Losada L. and S. Fernández W.—p. 524.

Pellagra in Adults.—Alessandri and his associates report observations on 110 cases of pellagra which were observed in Santiago de Chile between 1934 and 1941. Pellagra exists in Chile in the endemic as well as in the alcoholic and secondary forms. Twenty-nine of the patients presented the endemic form, 60 the alcoholic form; in the remaining 21 it was secondary to some grave organic disorder. Alcoholism and organic disease were etiologic factors. Pellagra has been increasing during the last five years. The authors calculate that in recent years Chile must have had about 3,000 cases of pellagra annually. In the city of Santiago twice as many cases were of alcoholic as of endemic origin. Endemic pellagra was more frequent in rural than in urban regions; this is so in Chile as well as in other countries. Women developed the endemic form more often than men. Alcoholic pellagra was three times more frequent in urban than in rural environment and appeared almost exclusively in men. Pellagra developed most frequently in persons between the ages of 30 and 60 years. Hospitalization for pellagra increased during the four hot months of the year. The total mortality for pellagra was 26 per cent in the reviewed material. In alcoholic pellagra the mortality was twice as high as in endemic pellagra. The authors discuss three groups of symptoms: (1) cutaneous, (2) nervous and mental disturbances and (3) digestive disorders. Until the beginning of 1939 the authors treated their patients according to Goldberg's recommendations with bed rest, a diet rich in antipellagral foods and yeast. In some cases antianemic hepatotherapy was employed with vitamin B or A. Since 1939 nicotinic acid has been added to the aforementioned treatment. Excellent results were obtained with the classic treatment of Goldberg in the majority of cases, but in some cases of extreme malnutrition this treatment has failed. The introduction of nicotinic acid signifies a definite advance in antipellagral treatment. It greatly accelerates recuperation, shortens hospitalization and thus reduces the expense of the treatment. The nicotinic acid is not, however, a substitute for the dietetic treatment but rather an important complement.

Thrombopenic Purpura Caused by Sulfonamide Compound.—Losada L. and Fernández W. report the history of a man, aged 60, who was given daily 3 Gm. of a sulfonamide compound for an injury to the left hand. Purpuric spots appeared on the fifth day of the treatment. There was a generalized purpura, most severe on the face, thrombopenia, lack of retraction of the clot, bleeding time of more than ten minutes and positive Rumpel-Leede sign. Puncture of the bone marrow disclosed hyporegeneration and immature platelets. Purpura is one of the late manifestations of intolerance to sulfonamide compounds. In this case it appeared on the fifth day of the medication. This can be explained by the fact that a sulfonamide compound exerts a toxic effect on the hemopoiesis in the bone marrow and does not affect the cells in the circulating blood, so that these retain for several days their normal proportion, the symptoms appearing days after the first ingestion of the drug. The authors have observed 2 other cases of purpura after sulfonamide medication: 1 a case of pneumonia in which sulfapyridine had been given and the other a case of typhoid in which sulfaguanidine had been given. All 3 cases took a favorable course. The treatment of this complication consists in discontinuing the drug, administering large doses of vitamin C and daily transfusions of from 100 to 150 cc. of blood.

Archiv für Gynäkologie, Berlin

172:1-160 (Oct. 16) 1941. **Partial Index**

Reduction of Prothrombin Effect by Anesthesia and Operation. W. Adams.—p. 87.
*Intensification of Action of Corpus Luteum by Vitamin E in Treatment of Habitual Abortion. E. Bach and H. Winkler.—p. 97.
Cause of Icterus Neonatorum. H. Albers.—p. 110.
Experimental Investigation on Modification of Uterine Muscle by Orally Active Corpus Luteum Hormone. E. Engelhart and P. Schrank. —p. 120.
Experimental Studies on Influence of Testosterone Propionate on Uterus. E. Engelhart and P. Schrank.—p. 129.
Gonadotropic Hormone in Placenta. W. Bickenbach.—p. 152.

Intensification of Corpus Luteum Action by Vitamin E in Treatment of Habitual Abortion.—Bach and Winkler report observations on 127 cases of threatened abortion treated by them during the years between 1930 and 1941. In 32 cases abortion took place. The authors differentiate four groups according to the treatment employed. The first group of 74 cases remained untreated and in 24 of these abortion resulted. In the second group of 27 cases progesterone was given and in 5 of these the treatment failed. A third group of 10 cases was treated with vitamin E; in this group there was 1 failure. In a fourth group of 16 cases vitamin E and progesterone were given; in this group there were 2 failures. Administration of progesterone has the effect of a substitutional therapy for an insufficient corpus luteum. Vitamin E intensifies the function of the corpus luteum not only by increasing the progesterone effect but also by a true activation, which is evidenced by the elimination of pregnandiol in the urine. The combined administration of vitamin E and progesterone unites the advantages of the two methods; the first doses of progesterone protect the pregnancy until the vitamin E can exert the intensifying effect on the corpus luteum, generally for a period of three days. The authors advise that the treatment be initiated with 10 mg. of progesterone, that this dose be reduced after three days and that it be broken off entirely after five days. The optimal daily dose of alpha tocopherol (vitamin E) is 30 mg. Lower doses activate the corpus luteum inadequately and only after a longer period. Doses in excess of 30 mg. do not increase the efficacy. Threatened abortions in women with definite infantilism in whom the elimination values of pregnandiol indicate not only an insufficiency in the follicular apparatus but also of the corpus luteum cannot be averted by beginning treatment during pregnancy. The initial values of pregnandiol elimination are far below normal, and the increase in function effected by alpha tocopherol is inadequate to maintain the pregnancy. The treatment to be successful in these cases must begin before the occurrence of pregnancy. Vitamin E is effective in increasing the production of progesterone and also in influencing growth of the fetus.

CORRECTION

Archiv für Gewerbepathologie, Berlin.—In the Current Medical Literature department of THE JOURNAL, January 2, page 86, the date of the issue of the foregoing German journal should have been April 16, 1941, instead of 1942.

Book Notices

New and Nonofficial Remedies, 1942. Containing Descriptions of the Articles Which Stand Accepted by the Council on Pharmacy and Chemistry of the American Medical Association on January 1, 1942. Austin E. Smith, M.D., C.M., M.Sc., editor. Issued under the direction and supervision of the Council on Pharmacy and Chemistry of the American Medical Association. Cloth. Price, $1.50. Pp. 608. Chicago: American Medical Association, 1942.

Perhaps the most important feature of this year's New and Nonofficial Remedies is the radical rearrangement. This should make the contents more accessible and therefore more valuable to the reader. Heretofore the classification of products has been basically that of chemical relationship—the new arrangement is primarily according to therapeutic use, chemical classification being introduced by means of subheadings. In addition, the typographic style has been changed to give greater prominence to the products of individual manufacturers. Valuable features have not been sacrificed. The book still fulfils its function of establishing chemical standards for new and nonofficial preparations which the Council has found to be useful or to give adequate promise of usefulness in the treatment or prevention of disease. Its function as a guide to the most recent advances in therapeutics has been greatly enhanced.

Careful examination of the general discussions under the various headings and subheadings shows that the Council has performed its annual task of keeping the text abreast of the progress of medicine. The authoritative and compendious section of the sulfonamide compounds is an example. So also is the chapter on vitamins and vitamin preparations for prophylactic and therapeutic use. Equally important though less extensive revisions have been made in such sections as those on aluminum compounds, dextrose, gonadotropic substances, liver and stomach preparations, ovaries, parathyroid, pituitary and testes.

Among the newly accepted drugs are:

Acetyl-Beta-Methylcholine and the proprietary brand, Mecholyl Chloride, proposed for use by iontophoresis, orally and subcutaneously as a parasympathetic stimulant.

Adrenal Cortex Extract for parenteral use in the treatment of Addison's disease or of adrenal insufficiency of other types as well as prophylactically in surgical procedures involving the adrenal cortex.

Aluminum Hydroxide Gel with the proprietary brand, Creamalin, for oral use as an adjunct in the treatment of peptic (gastric and duodenal) ulcer.

Normal Human Serum and Normal Human Plasma.

Others worthy of mention are:

Cyclopropane, another general anesthetic, now included in the U. S. Pharmacopeia.

Amylcaine Hydrochloride, another proprietary local anesthetic.

Pernoston Sodium, the sodium salt of the previously accepted proprietary barbital derivative, Pernoston.

This volume should be available to all medical students, physicians, pharmacists and others interested professionally or commercially in drug therapy. One cannot commend too highly the unselfish and untiring efforts of the Council on Pharmacy and Chemistry in the preparation of this invaluable contribution to rational and up to date therapeutics.

Drug Products: Labeling, Packaging, Regulation. By Arthur Donald Herrick, Member of the New York and Federal Bar. Fabrikold. Price, $7.50. Pp. 462, with 7 illustrations. New York: Revere Publishing Company, 1942.

Mr. Herrick has made a worth-while contribution toward orienting for the average reader the problems relating to the interstate sale of drugs and their advertising. This book is one which will be useful not only to those who are interested in interstate drug commerce but to the members of the medical profession and allied sciences who have a natural curiosity in the control of drugs. The contents include discussions on the early and present history of federal drug legislation, the Federal Food and Drugs Act, the Federal Food, Drug and Cosmetic Act of 1938, the formation of the Food and Drug Administration, products which are subject to the act, misbranded drug products, false and misleading labeling, packaged drug products, informative labels, label display and prominence, adequate directions and warning against misuse, fraudulent and dangerous drug products, products exempt from labeling, adulterated drug products, contaminated and harmful drug products, official drugs, maintenance of nonofficial standards, new drugs, submission, refusal and suspension of new drug applications, and cosmetics. A valuable portion of the book is contained in the appendixes, which include the Federal Food, Drug and Cosmetic Act, general regulations relating to drug products, U. S. Food and Drug Administration action on crude drugs, and U. S. Food and Drug Administration methods of testing antiseptics and disinfectants. The material is presented in an easily read style and represents the type of information which should be made generally available in view of the ever increasing interest in the control of drugs.

Report of the Committee on Tuberculosis in War-Time. Medical Research Council, Special Report Series No. 246. Paper. Price, 25 cents; 9d. Pp. 36. New York: British Information Service; London: His Majesty's Stationery Office, 1942.

Either the bovine or the human type of tubercle bacillus may give rise to disease in any part of the human body, and the type of infection can be determined only by careful bacteriologic examinations. In England and Wales, 98 to 99 per cent of all cases of pulmonary tuberculosis and 70 per cent of all cases of nonpulmonary tuberculosis are due to the human type of tubercle bacillus, and at all ages about 6 per cent of the deaths are due to the bovine type. In Scotland, however, the incidence of the bovine type of tuberculosis in man is higher than in England and Wales. Indeed, about 5 per cent of the cases of pulmonary tuberculosis are caused by the bovine type of tubercle bacillus. Because of the prevalence of both human and bovine tubercle bacilli in Great Britain, most persons come in contact with these organisms before they reach adult life and, therefore, practically all adults have at least the primary type of tuberculosis. Persons are liable to develop clinical tuberculosis either through fresh infections from the outside or from primary foci already established in their own bodies. Thus the situation in England varies definitely from that in the United States, where probably not more than 50 per cent of the entire population has been infected with tubercle bacilli and where in large areas this does not apply to more than 25 per cent. Moreover, in many parts of this country far more persons become infected in adult life than during childhood.

Tuberculosis mortality in Great Britain was gradually declining up to the beginning of the war. Indeed, between 1928 and 1938 the death rate in England and Wales was reduced from 91 to 60 per hundred thousand persons. Nevertheless, in 1938, 230,000 cases of clinical tuberculosis were under supervision of the dispensaries of England, Wales and Scotland. That year 65,000 new cases and 30,000 deaths were reported. In 1941 there was an increase of about 10 per cent in respiratory tuberculosis over that of the immediate prewar years in England and Wales, and about 18 per cent in Scotland. For nonrespiratory tuberculosis the increase was 21 per cent for England and Wales, and 28 per cent for Scotland. Thus, for all forms of tuberculosis the increased mortality was 13 per cent, or 3,780 actual deaths. In England and Wales the increase in respiratory tuberculosis affected mainly children, older men and younger women. However, the actual number of additional deaths among children has been much smaller than among adults in the case of respiratory tuberculosis.

The striking feature of nonrespiratory tuberculosis has been the increased incidence of tuberculous meningitis, which has affected all age groups up to 45. In children up to 10 years there has been a relative increase in mortality of 50 per cent.

While there were more actual deaths from tuberculosis during the first two years of the last war, the increase in mortality was 5 per cent for males and 7 per cent for females from 1914 to 1916, whereas in this war from 1939 to 1941 the increase has been 11 per cent for males and 13 per cent for females. During the last war children did not suffer appreciatively more from tuberculosis than in peacetime.

The authors call attention to the decline in mortality in Great Britain during the past eighty years. The lapse which occurred during 1914 to 1918 was thought to be due at that time to

unfavorable hygienic conditions, defective nutrition and increased industrialization. They believe that the greater prevalence of sources of human tuberculous infection has an important influence. Many tuberculosis hospitals and sanatoriums were evacuated in September 1939 to make room for expected air raid casualties. Thus large numbers of patients returned to their homes while the disease was contagious. Blackout conditions, with diminished ventilation and increase in cross infection, overcrowding in homes due to destruction of residential property by enemy action and the added effects of billeting, evacuation of the population which may have led to billeting in homes containing infective tuberculous persons, and also the introduction of tuberculous persons into healthy homes, are thought to have played an important part in spreading tuberculosis. The evacuation of town populations to the country, with the result that many children previously supplied with pasteurized milk were then supplied with raw milk, is also considered significant. Therefore all ages of the population are being subjected to an increased risk of exposure to tuberculosis.

Apparently large numbers of persons working in factories have been exposed to fellow workers with contagious tuberculosis, since the demand for more labor has brought into activity many persons who in peacetime would not be working.

The following measures for the prevention of further increase in tuberculosis are discussed: The first consideration in this respect is to reduce the spread of bovine infection from dairy products. Tuberculosis is widespread among the cattle of Great Britain. Before the present war began about 40 per cent reacted to tuberculin, and 40 per cent of those slaughtered in the abattoirs had areas of disease sufficiently large to be seen with the naked eye. Five-tenths per cent of milch cows were eliminating tubercle bacilli through the milk. Over 6 per cent of all farms were sending out milk containing living tubercle bacilli. In 1937 the Ministry of Agriculture introduced a plan for controlling tuberculosis in cattle, but by 1939 only about 3 per cent of the dairy farms had their herds attested. Unfortunately, this plan had to be practically abandoned during the war and there seems no hope that further progress in the eradication of tuberculous infection from cattle can be expected until more normal conditions are restored. Therefore the milk will continue to contain tubercle bacilli and the only possible immediate solution is to destroy them by heat. The authors give various suggestions for pasteurization in towns and cities and educating housewives elsewhere to heat milk adequately.

The unsuspected case of tuberculosis is regarded as a significant factor in the increase of the disease during the present war. Symptoms usually appear late, and therefore most patients have moderately or far advanced disease when it is diagnosed. The authors believe that these unsuspected cases should be screened from those sections of the population where there is the greatest danger of spreading disease. For this purpose they recommend mass radiography. They feel that the miniature film is the best solution of the present problem because of the extremely low cost and the speed with which it can be processed. However, they are thoroughly cognizant of the fact that this is not the ideal method of doing x-ray work nor is it the fastest. They recommend mass radiography as a preemployment procedure and one which should be extended to all persons employed in certain industries. They also believe it should be a periodic requirement because they are cognizant of the fact that persons whose chest films may be clear on first examination may at any subsequent time present evidence of disease.

In administering the proper treatment of persons with tuberculosis the authors lament the fact that the number of beds in sanatoriums has been decreased and that nurses and physicians are difficult to obtain for the care of the tuberculous. All this adds significantly to the problem.

Some American workers will take issue with the statement that the risk of infection with tuberculosis from nursing tuberculous patients in sanatoriums is no greater than that involved in general hospital nursing.

The committee recommends a plan whereby the patient is allowed sufficient financial support for himself and his family until he is able to resume his work. It recommends a number of schemes for providing work for persons with the disease in a quiescent noninfectious stage on a part time basis. It also calls attention to an extremely important special group, namely persons with chronic contagious tuberculosis who cannot be treated so as to render them noncontagious and yet are not seriously ill. Many of them have good working capacity either on a part time or a full time basis. It is believed that these persons could be employed in groups where they will not disseminate their tubercle bacilli to others.

The section on tuberculosis in institutions for the mentally ill is intensely interesting and throws further light on the real cause of the increase in tuberculosis during wartime. In peacetime the mortality rates from tuberculosis in these institutions was eight or nine times that of the general population. Between 1910 and 1914 it varied between 15 and 17 per thousand resident patients but during the last war it rose to 37 per thousand in 1917, and 52 per thousand in 1918. A similar trend is already apparent in the present war, and this applies also to the institutions for mental deficiency. During the last war it was thought that the increased mortality was largely due to insufficient diet, but the authors are not prepared to pass the same judgment now, because both the quantity and the quality of the food has been good in these institutions in this war. On the other hand, there has been definite overcrowding, which has apparently increased infection possibilities from contagious cases.

A concise summary of findings and recommendations by the members of the council is included. The report contains an unusually modern point of view on tuberculosis control which is applicable to any nation where nearly all of the adult population is infected with tubercle bacilli.

Ultra-Violet Light and Its Applications Including a Description of the Numerous Practical Applications Found for Ultraviolet Light and Fluorescence in the Industries, Sciences, and Arts. By H. C. Dake and Jack De Ment. Cloth. Price, $3.25. Pp. 209, with illustrations. Brooklyn & New York: Chemical Publishing Company, Inc., 1942.

This volume deals largely with the utilization of ultraviolet radiation in commercial and technical applications. One chapter is devoted to medical sciences, and it stresses the employment of ultraviolet radiation in diagnostic procedures. Little or nothing is written on therapeutic applications of ultraviolet radiation. There are many clever ideas suggested for using ultraviolet radiation in the practice of surgery, bacteriology, dermatology and pharmacology. How diseased tissues will fluoresce in the presence of ultraviolet is described, and valuable hints are advanced for the technic of recognizing pathologic tissues. The significance of ultraviolet radiation in bacteriology utilizing microinjections of fluorescent dyes and the colors certain organic and inorganic chemical compounds will produce under the influence of ultraviolet radiation are described. At least half of the book is devoted to the uses of ultraviolet radiation in criminology and police science, military, advertising, theatrical, mining and oil drilling applications. A list of firms is recorded at which supplies may be obtained for use in ultraviolet and fluorescent practice.

Clinical Thermometers: A Recorded Voluntary Standard of the Trade. Commercial Standard CS1-42. U. S. Department of Commerce, Jesse H. Jones, Secretary, National Bureau of Standards, Lyman J. Briggs, Director. Third edition. Paper. Price, 10 cents. Pp. 19. Washington, D. C.: Supt. of Doc., Government Printing Office, 1942.

This pamphlet describes approved methods for testing clinical thermometers. The National Bureau of Standards in 1927 was requested by a committee of the Associated Thermometers Manufacturers to assist in establishing a commercial standard for clinical thermometers, to encourage the production and sale of reliable thermometers and to protect purchasers from inferior and unreliable instruments. The proposed standards were drafted and adopted in 1928. The first revision was in 1931 and the second revision in 1940. In order to be accepted, thermometers must meet standards of construction, aging, pigment tests and tests for entrapped gas and accuracy. There are tests for "hard shakers" and for "retreating index." For the accuracy test, thermometers are compared at 98, 102 and 106 F. and must be tested in a certain prescribed way as explained in the pamphlet. Rigid tolerances of accuracy are demanded. The bureau is to be congratulated for its efforts in assuring accurate thermometers for the profession.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

DERMATITIS FROM CUTTING OILS

To the Editor:—**The matter of dermatoses in men in munitions factories working with water soluble oils becomes an acute one. In a certain factory there is in use a preventive, Steridol number 3, made by the C. B. Dolge Company of Bridgeport, Conn. Will you give me information concerning this product and about the matter of these dermatoses and the pertaining bibliography?**

M.D., Michigan.

ANSWER.—The large majority of cutting oil dermatitis occurs from the insoluble cutting oils, yet these are sterile as far as pathogenic bacteria are concerned. Only a comparatively small percentage of dermatitis from cutting oils is caused by the water soluble cutting oils, which, in contradistinction to the insoluble oils, usually contain many pathogenic bacteria. Usually they also have an offensive odor and may contain metal slivers. It is possible to have the skin injured by the slivers and the cut become infected from the bacteria in the water soluble oil or on the soiled skin and clothing.

Sedimentation and filtration to remove the chips and pasteurization to kill the bacteria are used in many plants where the water soluble oils are reclaimed and circulated through a sterilization system. In plants where pasteurization systems are not installed, antiseptics can be used in order to destroy the bacteria in soluble cutting oils.

Steridol number 3, sold by the Dolge Company, is one of these antiseptics. The extract composition of Steridol is not given by the manufacturers, but it is believed to be of the formaldehyde type of disinfectants.

The advantage claimed for disinfectants in cutting oils over heat sterilization is that when disinfectants are used the oil cannot be reinfected in the pipes and at the machines. The disadvantage of disinfectants is that they are all skin irritants and increase the dermatitis hazard from the cutting oils. Especially is this so because the continued addition of disinfectants to cutting oils for the purpose either of disinfecting them or of destroying or masking the objectionable odors (caused by the formation of sulfur compounds) has been known in some instances to increase the disinfectant content of such oils to as high as 5 per cent.

The claims made for Steridol can be read in a booklet entitled "Cutting Oil Sanitation," issued by the C. B. Dolge Company, Westport, Conn. For further reference to this subject see "Dermatitis from Cutting Oils" by Louis Schwartz (*Pub. Health Rep.* **56**:1947 [Oct. 3] 1941, reprint 2321).

ANATOMY OF LEFT PLEURAL CAVITY

To the Editor:—**In answer to M.D., Utah (The Journal, May 9, 1942, p. 232), there appears the following statement: "The left pleural cavity largely drains via the vena azygos minor, which usually empties into the left innominate vein and so is not so immediately obstructed as is the vena azygos major." According to all recent textbooks of anatomy in the English language (Piersol, ninth edition, 1930, p. 895; Morris, ninth edition, 1933, pp. 735-736; Cunningham, seventh edition, 1937, p. 1241; Gray, twenty-second edition, 1930, p. 668) and personal observations, both vena azygos minor inferior and vena azygos minor superior empty into the vena azygos major. The left superior or highest intercostal vein, which drains the blood from the upper three or four intercostal spaces, opens into the left innominate vein. The left superior intercostal vein often communicates with the left vena azygos minor superior and may drain a small amount of blood from the highest part of the parietal pleura on that side. The statement from The Journal quoted does not seem to agree with the anatomic findings; therefore it should not go unchallenged.**

K. S. Chouké, M.D., Philadelphia.

ANSWER.—The challenge to the statement in THE JOURNAL concerning the preponderance of right hydrothorax in congestive heart failure is well taken and indicates the need of elucidation. There should be a correction of the statement to read as follows: "Drainage from the left pleural cavity is by way of the hemiazygos (azygos minor inferior) and accessory hemiazygos (azygos minor superior) veins, the latter not only emptying into the vena azygos major but also anastomosing almost always with the left innominate vein, which connection may account for the lesser degree of venous obstruction on the left side than on the right."

DIFFERENTIAL DIAGNOSIS OF BACKACHE

To the Editor:—**I am 32 years old, well nourished, weigh 164 pounds (74 Kg.), am 5 feet 8 inches (173 cm.) tall and have suffered from flat feet for the last fourteen years. From the beginning I have had good medical care with regard to my arches. However, I have always had trouble with my arch supports, which for the most part were made of aluminum covered with leather. On the average I had new ones made every one or two years; at the same time I had to go back to the orthopedic mechanic constantly for adjustments, for they never felt completely satisfactory. Nevertheless I managed to get by somehow through a one year internship from 1937 to 1938, despite the fact that at this time my assisting in the operating room gave me sacroiliac backaches. During this time I saw many orthopedic surgeons. Exactly one year ago I decided to move my office from New Jersey to upstate New York. During this period I was busy packing and lifting heavy packages, cartons and the like. After I had my work almost completed I suffered a sudden attack of upper back pain, dull, not radiating, in the middle, at the height of the seventh to tenth dorsal vertebrae. A well trained orthopedic surgeon ordered me to have a few days of bed rest, after which I received a series of treatments which consisted of diathermy and massages of my back. I also exercised at home to straighten my posture and to increase my muscle tonus, which is rather flabby because of the fact that I never had much of a chance to indulge in sports. My backaches were improved for a short time only to return again, and for the last ten months I have never been without backache for more than a period of four or five days; then they always recur. I have consulted several orthopedic specialists without any success. My backaches always improve temporarily after my back is massaged. For this reason I had no roentgenograms taken. Please advise me of the possible diagnosis and treatment and, mainly, please give me the names of a few authorities in this field, preferably in the East.**

M.D., New York.

ANSWER.—A differental diagnosis of backache such as described could not be made without additional information. Chronic malposture may result, in time, in producing symptoms of strain or wear and tear arthritis in the articular facets of the spine. Degenerative changes in the intervertebral disks secondary to an old healed vertebral epiphysitis are occasionally seen and are most often present in the lower thoracic spine. Herniation of an intervertebral disk may result from a lifting strain such as that which has been described.

Roentgenograms of the spine should be made. A careful neurologic examination is important. A therapeutic test of support by means of a good back brace may be helpful. As a number of competent orthopedic surgeons have already been consulted, it would appear to be advisable that a consultation should be arranged between an able orthopedic specialist and a neurologist. Perhaps a spinal puncture would be found to be indicated.

There is no one leading authority in this particular field in the big Eastern cities who is preeminently superior to other good orthopedic surgeons in the same locations.

POSTPARTUM CARE

To the Editor:—**Will you give me the current opinion regarding: (1) the routine use of shock blocks following delivery, (2) postpartum laxatives for the mother and (3) the use of ergot or a similar preparation for the first twenty-four to seventy-two hours post-partum?**

R. F. DeWitt, M.D., Plymouth, N. H.

ANSWER.—1. There is no indication for the routine use of shock blocks following normal delivery. This is one of the procedures that should be reserved for the patient who has had excessive loss of blood.

2. Almost all mothers need a mild laxative following delivery, although there has been much abuse in the use of laxatives. For the patient who has had a natural delivery without perineal repair, liquid petrolatum can be started on the second day and if necessary a small tap water enema can be administered the third morning. The liquid petrolatum can be continued while the patient is in bed or an agar in oil preparation can be substituted. If the patient does not have a bowel movement, the small tap water enema can be repeated every other day. For the patient who has had an episiotomy, oil can be started on the second day and in the absence of a bowel movement the tap water enema can be administered on the morning of the fourth day. For the patient who has sustained an injury to the anal sphincter, the administration of liquid petrolatum can begin on the fourth morning, a small oil retention enema can be given the evening of the fifth day, and if there is no bowel movement this can be followed by a small tap water enema the following morning. This routine has provided satisfactory results in a large obstetric service.

3. It is the practice in many large institutions to administer a 0.2 mg. tablet of ergonovine two or three times a day during the first seventy-two hours to all patients. Severe after-pains may warrant discontinuing the oxytocic drug. In the presence of infection or retarded uterine involution from some other cause, ergonovine can be continued for a longer period.

EPINEPHRINE AND PROCAINE SOLUTIONS IN DENTAL SURGERY

To the Editor:—Several misinterpretations appear in reply to the query concerning the addition of epinephrine to the procaine solution used in dental operations (The Journal, Sept. 19, 1942, p. 248). Dentists seldom employ epinephrine for the purpose of securing a dry field; if they should, their success would be indifferent. While it appears that procaine hydrochloride alone is an adequate obtundent for the surgical manipulation of soft tissues, it is unquestionable that anesthesia of far greater depth is required to eliminate sensation in the parodontal tissues, and especially the dental pulp. Experience has repeatedly shown that this is rarely secured without the addition of a vasoconstrictor, which functions chiefly to intensify the action of the procaine by retarding its absorption. This becomes increasingly true in employing the nerve blocking method, which is mandatory in anesthetizing the lower posterior teeth. Satisfactory operating results in these areas virtually never follow the use of procaine alone. Optimum effects require a concentration greater than 1:75,000 of epinephrine, greater than 1: 80 of procaine hydrochloride, as well as a waiting period of over ten minutes to allow anesthesia to reach a satisfactory depth. Many thousands of patients with anginal syndromes have been injected with 2 to 3 cc. of such concentrations both in the hospital and in the dental office without encountering severe reactions, if the principle of basal anesthesia with barbiturates is employed and the solution is injected extremely slowly, with the patient supine. Moderate reactions may occur, as they do in other groups of patients, but they are generally transitory and negligible. Nevertheless, caution dictates that glyceryl trinitrate and other restoratives are at hand to anticipate an emergency. The answer to the problem posed would seem to be that the patient who is a poor risk for the anesthetic is likewise a poor risk for the extraction. Excepting for the relief of intractable pain, the operation should be postponed until the clinical condition offers a proper margin of safety or perhaps be altogether avoided by compromise treatment. Even under favorable circumstances, extraction is a procedure not devoid of hazards and should be approached with the same careful judgment as any other operative measure.

Leo Stern, D.D.S., New York.

To the Editor:—In Queries and Minor Notes in The Journal, Sept. 19, 1942, page 248, there is a question about the use of procaine hydrochloride with and without epinephrine when dealing with the anginal syndrome. In the reply it is stated that either epinephrine is omitted in certain cases or cobefrin is used in place of it. It should be noted that clinical and experimental evidence shows that cobefrin is subject to the same disadvantages as epinephrine.

Isaac Neuwirth, New York.

Associate professor of
pharmacology and therapeutics,
New York University College of Dentistry.

ANSWER.—[These two letters were referred to the consultant who replied to the original query. His reply follows.] I still believe that the original answer is correct. It could have been amplified to include the effect of preliminary medication, skill in injection, the patient's disability, his nervousness and his output of epinephrine, but briefness was indicated. I generally employ cobefrin in a dilution of 1 : 5000 as compared to epinephrine in a dilution of 1 : 150,000. Epinephrine in this dilution causes constriction of peripheral blood vessels and thus produces a fairly dry field.

Under these conditions, obviously, absorption of the anesthetic solution is slowed and anesthetic solution is not lost by hemorrhage. Therefore anesthesia is considerably prolonged. Nevertheless, I see fewer untoward effects with cobefirin than with epinephrine and, under the conditions with which this correspondence deals, I prefer cobefrin.

DIETHYLSTILBESTROL AND HAIR LOSS

To the Editor:—Can diethylstilbestrol cause the loss of hair from the scalp? A woman aged 22 never had a period previous to December 1941. She had had bilateral mumps at the age of 10. The uterus was small, the breasts were infantile in type, and there was a definite masculine hirsutism. With diethylstilbestrol, which she has been taking since December 1941, periods have been at regular intervals and the dose of diethylstilbestrol has been regulated so as to have the periods at intervals of four weeks. The monthly dose was 1 mg. daily for five days and 2 mg. daily for another five days. In July she felt much better, and I had not seen her again for three months. She still feels well but has skipped the last two periods; practically all evidence of masculine hirsutism has disappeared and the scalp is noticeably bald, especially in the region of the temples. I have noticed changes in the distribution of hair (possibly coincidental) with other estrogens, but nothing so severe. The basal metabolic rate was minus 11 per cent in February. The blood pressure was 160 mm. systolic (following the death of a relative) but has now been normal since April. An organic basis for the blood pressure could not be found from pyelogram and urine cultures; the urea clearance test was normal.

M.D., Massachusetts.

ANSWER.—As far as is known there is no connection whatever between the loss of the hair from the scalp and the ingestion of diethylstilbestrol. The condition in the case cited would appear to be coincidental.

SYMPATHETIC AND PARASYMPATHETIC NERVE SUPPLY OF CEREBRAL VESSELS

To the Editor:—Would you please inform me whether stimulation of the sympathetic nerves leading to brain vessels produces vasoconstriction or vasodilatation? Have any sympathetic vasodilator nerves in the cerebral vessels ever been found? Can acetylcholine act on the cerebral blood vessels producing vasodilatation, and, if so, where does the acetylcholine develop, since there are no parasympathetic fibers present?

M.D., New York.

ANSWER.—Stimulation of one cervical sympathetic trunk produces feeble constriction of the pial blood vessels on the same side of the brain. Other nerve fibers reach the arteries of the brain stem from the facial nerve by way of the greater superficial petrosal branch. The last mentioned group of fibers are commonly referred to as parasympathetic. Stimulation of this group gives feeble dilatation of the blood vessels of the ipsilateral cerebral cortex. Acetylcholine produces moderate dilatation of the pial vessels. It may be assumed to develop at the so-called parasympathetic endings. In reality, the presence of parasympathetic vasodilator nerves has never been satisfactorily proved. It is probable that sympathetic nerves normally control both the constriction and the dilatation of blood vessels. It is true that stimulation of the peripheral ends of divided posterior nerve roots produces vasodilatation. This may be an abnormal antidromic effect releasing a chemical mediator at the sensory nerve ending on the blood vessel.

BIOLOGICALLY FALSE SEROLOGIC TESTS

To the Editor:—A white woman aged 30, in excellent health, presented herself for a routine blood test. She is unmarried and denies any possible exposure to syphilis by sexual intercourse. Physical examination and history are negative for symptoms and signs ordinarily attributed to a syphilitic infection. The history is extremely reliable in this instance. There is no history of previous infection or treatment for syphilis. A spinal fluid test has not been done.

Results of the Blood Tests

Date	Laboratory	Kline	Kahn	Kolmer	Kahn Verification Test
6-25-42	1	Positive	Neg.	2+	Not done
7- 2-42	1	Positive	Neg.	2+	Not done
7- 6-42	1	3+	±	Negative	Not done
7- 6-42	2	Not done	Neg.	Not done	Negative
7- 6-42	3	Not done	±	Negative	
		Eagle, Mazinni done by this laboratory were negative. Hinton was doubtful.			
8-11-42	1	Not done	Neg.	4+	Not done
10- 3-42	1	Not done	Neg.	Negative	Not done
10-16-42	1	Not done	Atypical reaction	Negative	Not done

This patient is now under my supervision. No antisyphilitic treatment has been given. Suggestions on the handling and further study of this case will be appreciated.

Don V. Hatton, M.D., Fayetteville, W. Va.

ANSWER.—The conflicting serologic reports obtained thus far in this case do not warrant a diagnosis of syphilis and appear to be of the so-called biologically false positive type. The things that make these reports appear to be "false positive" are the inconsistency in the positive tests by different technics, the variation in the degree of positiveness and the variation in the tests done on the same specimen of blood by three different laboratories. In view of these findings, a diagnosis of syphilis is not justified and accordingly treatment of this young woman for the disease is not warranted. A spinal fluid examination should be made because a positive report will sometimes be found even though the tests of the blood are as conflicting as in this case. If the spinal tests are negative, the future procedure would be to recheck the tests at two to three month intervals and when so doing to reexamine the patient for evidence of syphilis. It is not uncommon that false positive tests will spontaneously revert to negative and remain so when rechecking of the tests is done over a period of a year or so. If the spinal reports are positive, treatment for syphilis would then be warranted.

Numerous factors enter into the creating of the false positive test, among which are recent influenzal infections, low grade febrile conditions, glandular tuberculosis, disseminated lupus erythematosus, pastvaccination against smallpox, typhoid and drawing the specimen during the menstrual period. These are among some of the more recently found causes for unsatisfactory serologic tests such as the example given.